

ATTORNEY'S DOCKET NUMBER: 0492479-0018 (MGH 1661.0)

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant: Scadden *et al.*  
Serial No.: 09/803,687  
Filed: March 9, 2001  
For: *p27 and p21 in Gene Therapies*

Examiner: Katcheves, K. T.  
Art Unit: 1636

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

**DECLARATION UNDER 37 C.F.R. § 1.132**

I, David T. Scadden, declare as follows:

1. I am an inventor of the subject matter disclosed and claimed in United States patent application, Serial Number 09/803,687, filed March 9, 2001, and entitled "p27 and p21 in Gene Therapies."
2. I am a Professor in the Department of Medicine at Harvard University. I also serve as Co-director of the Harvard Stem Cell Initiative, Director of the Center for Regenerative Medicine and Technology at the Massachusetts General Hospital (MGH), and Chief of Hematologic Malignancies at the MGH. The MGH is the assignee of the above-referenced patent application. My research has focused on stem cell biology, particularly of hematopoietic stem cells, including entry and exit from the cell cycle with implication for stem cell expansion and gene transduction. A copy of my curriculum vitae is attached hereto as **Appendix A**.
3. I have read the Office Action mailed December 23, 2004, and understand that the Examiner requests further evidence regarding the invention as claimed in the present application

and specifically as it pertains to the ability of one to use antisense agents and RNAi agents in expanding a population of stem or progenitor cells based on the disclosure of the application.

4. My research group has previously shown that p21<sup>Waf1/Cip1/Sdi1</sup> (p21) mediates stem cell quiescence *in vivo* and decreasing p21 expression leads to an expansion of the stem cell pool. We have now demonstrated that p21 specific siRNA agents increase the gene transduction efficiency in hematopoietic stem cells while preserving cell multipotentiality.

5. Two types of RNAi were generated to silence p21 expression in target cells—*in vitro* synthesized duplex siRNA and *in vivo* expressed plasmid-derived short hairpin RNA (shRNA). See **Appendix B**. The effects of silencing p21 were studied in primary human CD34+ hematopoietic stem/progenitor cells and CMK cells derived from human megakaryoblastic cells.

6. Both types of siRNA (Si-2 and p2.3) knocked down p21 expression by 85-98% as measured with p21 mRNA copy number using real time RT-PCR. A mismatched mutant siRNA (Si-2M) served as a specificity control and did not affect p21 expression. The RNAi effect on mRNA levels was confirmed by reduced p21 protein levels as demonstrated by Western blot. See **Appendix C**.

7. For synthesized siRNA, the level of p21 mRNA returned to baseline at 10-15 days post siRNA treatment, and for transcribed shRNA derived from the plasmid, the level of p21 mRNA was back to the pre-silencing level at 22-28 days post treatment. See **Appendix D**. Silencing p21 in a transient manner by siRNA is appealing because it limits the potential for permanent p21 deficiency contributing to malignant transformation.

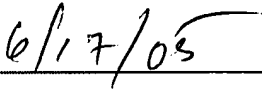
8. Silencing p21 increased the efficiency of gene transduction in CD34+ hematopoietic stem/progenitor cells and preserved the multipotentiality of these cells while allowing for stable integration of gene transfer-vector into the cellular genome. Silencing p21 using RNAi may ultimately contribute to the clinical application of gene therapy in hematopoietic stem cells.

9. The data presented in the Declaration was accepted on March 17, 2005 for publication in *Gene Therapy*. The manuscript is currently in press.

10. I, David T. Scadden, declare that all statements made herein of my own knowledge are true and that these statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful, false statements and the like are made punishable by fine or imprisonment, or both, under § 1001 of Title 18 of the United States Code and that such willful, false statements may jeopardize the validity of the application or any patents that may issue thereon.



David T. Scadden, M.D.



Date



## APPENDIX A

## CURRICULUM VITAE

### PART I: General Information

**DATE PREPARED:** Last updated 5/25/05 by CP

**Name:** David T. Scadden, M.D.

**Office Address:** 185 Cambridge Street, CPZN 4265A, Boston, MA. 02114

**Office Telephone:** (617) 726-5615

**Home Address:** 62 Lexington Street, Weston, MA. 02193

**E-Mail:** [scadden.david@mgh.harvard.edu](mailto:scadden.david@mgh.harvard.edu) **FAX:** (617) 726-2662

**Place of Birth:** Passaic, New Jersey

### Education:

1975	B.A.	Bucknell University (English)
1975-1976		Columbia University (Pre-Medical Studies)
1980	M.D.	Case Western Reserve School of Medicine
2004	A.M.	Harvard Medical School (Honorary)

### Postdoctoral Training:

#### Internship and Residencies:

1980-1981	Intern	Brigham and Women's Hospital, Boston, MA.
1981-1982	2 <sup>nd</sup> year Medical Resident	Brigham and Women's Hospital, Boston, MA.
1982-1983	3 <sup>rd</sup> year Medical Resident	Brigham and Women's Hospital, Boston, MA.

#### Clinical and Research Fellowships:

1980-1984	Clinical Fellow in Medicine	Harvard Medical School
1983-1984	Clinical Fellow in Hematology/Oncology	Brigham and Women's Hospital, Dana-Farber Cancer Institute
1984-1986	Research Fellow in Medicine	Harvard Medical School
1985-1987	Research/Clinical Fellow in Medicine	Brigham and Women's Hospital (JM Cunningham, mentor)
1987-1988	Research Fellow	New England Medical Center (RS Schwartz & JM Coffin, mentors)

### Licensure and Certification:

1980	Diplomate, National Board of Medical Examiners
1983	Massachusetts License Registration
1983	Diplomate, American Board of Internal Medicine
1985	Diplomate, Subspecialty Board in Medical Oncology
1988	Diplomate, Subspecialty Board in Hematology

#### **Academic Appointments:**

1986-1987	Instructor in Medicine	Harvard Medical School
1987-1988	Instructor in Medicine	Tufts University School of Medicine
1988-1991	Instructor in Medicine	Harvard Medical School
1991-1995	Assistant Professor of Medicine	Harvard Medical School
1995-2003	Associate Professor of Medicine	Harvard Medical School
2003-	Professor of Medicine	Harvard Medical School, Harvard University

#### **Hospital or Affiliated Institution Appointments:**

1988-1996	Active Staff	Deaconess Hospital, Boston, MA.
1988-1993	Courtesy Staff	St. Luke's Hospital of New Bedford, MA.
1995-1996	Courtesy Staff	Waltham-Weston Hospital, Waltham, MA.
1995-2001	Associate Physician	Massachusetts General Hospital, Boston, MA.
1997-2005	Staff Physician, Hematology/Oncology	Brigham and Women's Hospital, Boston, MA.
1997-	Staff Physician, Hematology/Oncology	Dana-Farber Cancer Institute, Boston, MA.
2001-	Physician	Massachusetts General Hospital, Boston, MA.

#### **Other Professional Positions and Major Visiting Appointments:**

1985-1987	Associate	Howard Hughes Medical Institute, Boston, MA
-----------	-----------	---------------------------------------------

#### **Major Administrative Responsibilities:**

1993-1995	Director, AIDS Hematology/Oncology Research Unit, Deaconess Hospital
1995-	Director, Experimental Hematology, Massachusetts General Hospital
1995-2004	Co-Director, AIDS Research Center, Massachusetts General Hospital
1995-1997	Mentoring Committee, Dana-Farber/Partners Cancer Care
1996-	Chair, Immunodeficiency Disease Center, Dana-Farber/Partners Cancer Care
1996-2000	Steering Committee, Hematologic Malignancies, Dana-Farber/Partners Cancer Care
1996-2001	Scientific Review Committee, Dana-Farber/Partners Cancer Care
1996-1999	Mallinckrodt General Clinical Research Center (GCRC) Advisory Committee Member, Massachusetts General Hospital
1997-1998	Fellowship Selection Committee, Hematology/Oncology, Dana-Farber/Partners Cancer Care
1998-	Committee of Immunology, Harvard Medical School, Program in Immunology
1999-	External Advisory Committee, The Connell O'Reilly Cell Manipulation and Gene Transfer Laboratory, Dana-Farber Harvard Comprehensive Cancer Center
2000-	Chair, Oncology Clinical Recruitment Committee, Massachusetts General Hospital

2000- Director, Hematologic Malignancies Program, Massachusetts General Hospital  
2000- Co-director, Partners/Fenway/Shattuck Center for AIDS Research  
2000-2001 Intern Selection Committee, Massachusetts General Hospital  
2000-2004 Executive Committee Member, Harvard Medical School Division of AIDS (HMSAIDS)  
2001- Cancer Center Advisory Board, Massachusetts General Hospital Cancer Center  
2002- Member, National Cancer Institute Board of Scientific Counselors, National Institutes of Health  
2002- Director, Center for Regenerative Medicine and Technology, Massachusetts General Hospital  
2004- Co-Director, Harvard Stem Cell Institute, Harvard University  
2005- Member, Biological and Biomedical Sciences Program, Harvard Medical School

### Major Committee Assignments:

1990 Ad hoc review committee, "Clinical Research in AIDS", National Institutes of Health  
1993-1995 Oncology Core Committee, ACTG, NAIAD  
1994 Ad hoc review committee, "Basic Research on Hematopoietic Stem Cell Biology", National Institute on Diabetes and Digestive and Kidney Diseases  
1994 Ad hoc review committee, "Studies of the viral etiology of AIDS-associated malignancies", National Cancer Institute  
1994-1995 Research Agenda Committee, ACTG, NIAID, "Complications of HIV."  
1995 Ad hoc review committee, "Cytokines Effects on Hematopoiesis in AIDS Animal Models", National Heart, Lung, and Blood Institute  
1995-present AIDS Malignancy Consortium, Steering Committee, National Cancer Institute  
1995-1999 AIDS Malignancy Consortium, Lymphoma Working Group, Chair, National Cancer Institute  
1996 Ad hoc reviewer, National Heart, Lung, and Blood Institute, Hematology 2 Study Section  
1996-2000 AIDS Malignancy Working Group, Chair, Clinical Investigation, National Cancer Institute  
1997 Ad hoc reviewer, Hematology-2 Study Section, National Institutes of Health  
1998 Task Force on Integration of Adult HIV/AIDS Clinical Trials Networks, Office of AIDS Research, National Institutes of Health  
1998 DaunoXome and AmBisome Advisory Board, NeXstar Pharmaceutical  
1998 External Advisory Board, University of Colorado BMT Program Project  
1998 Advisory Board, HMS SCOR in Hematologic Disease  
1998- Scientific Review Committee, Member, Concert for the Cure, Boston, MA  
1998 Outside Reviewer, Dutch Cancer Society  
1999 Program Project Review Committee, Member, National Institutes of Health  
1999 Ad hoc Scientific Review Committee, Member, National Institutes of Health, "Clinical Research Studies."  
2000- AIDS Malignancy Consortium, Executive Committee, Chair, National Cancer Institute  
2000 Site Visit Team, Member, HIV/AIDS Malignancy Branch, National Institutes of Health  
2000 Finance Task Force, Committee Member, American Society of Hematology

2000 Site Visit Team Member, NCI Medicine Branch, Department of Experimental Transplantation and Immunology, National Institutes of Health

2000 Steering Committee Member, AFM/Harvathon Gene Therapy Initiative

2001 Etiology and Pathogenesis Planning Workshop Member, FY 2003 NIH Plan for HIV-Related Research, Office of AIDS Research, National Institutes of Health

2001 Outside Reviewer, Hematology-2 Study Section, National Institutes of Health

2001 Outside Reviewer, AIDS and Related Research-6, National Institutes of Health

2001 Outside Reviewer, Wellcome Trust

2001- Standing Review Panel, Member, Doris Duke Charitable Foundation's Clinical Scientist Development Award Program

2001-2004 Committee on Investment & Audit, Member, American Society of Hematology

2001 Outside Reviewer, AIDS Research Review Committee, National Institute of Allergy and Infectious Disease, National Institutes of Health

2001- Ad hoc Clinical Search Committee, Brigham and Women's Infectious Disease Division, Partners AIDS Research Program

2001 Honorary Consultant, Chinese Foundation for Prevention of STD and AIDS

2002- AIDS Malignancy Lab Working Group, Co-Chair, Clinical Investigation, National Cancer Institute

2002 Honorary Consultant, Institute of Hematology, Tianjin, China

2002 Grant Review Committee Chair, National Cancer Institute of Canada

2002- Scientific Advisory Board member, Harvard Gene Therapy Initiative

2003 Scientific Advisory Board member, Center for Cutaneous Biology, Massachusetts General Hospital

2003- Ad hoc recruitment committee, Hematology Division, Brigham & Women's Hospital

2003- Ad hoc recruitment committee for Assistant Director, Blood Transfusion Service, Massachusetts General Hospital

2003- Ad hoc recruitment committee for Director, Wellman Labs, Massachusetts General Hospital

2003- Ad hoc recruitment committee for Director, Hematologic Malignancies, Massachusetts General Hospital and Professor, Harvard Medical School

2003 Site Visit Team, Member, Viral Epidemiology Branch, National Institutes of Health

2003- Immunology Scientific Advisory Board member, New England Primate Research Center, Harvard Medical School

2004- Data Safety Management Board, Alexion Pharmaceuticals

2004 Panel Member, Tumor Stem Cells and the Genetic Basis of Self Renewal Think Tank, National Cancer Institute, National Institutes of Health

2004 Site Visit Team, Chair, HIV/AIDS Malignancy Branch, National Institutes of Health

2004-2005 Member, Committee on Establishing a National Cord Blood Stem Cell Bank Program, Institute of Medicine, The National Academies

2004- Ad hoc faculty search committee for Center for Human Genetic Research, Massachusetts General Hospital and Associate Professor, Harvard Medical School

2004- Ad hoc faculty search committee for New England Primate Research Center, Harvard Medical School and Assistant Professor, Harvard Medical School

2004- Ad hoc faculty search committee for Cardiovascular Division, Brigham & Women's Hospital and Professor of Medicine, Harvard Medical School

2004- Member, Advisory Board, International Society for Stem Cell Research



2005- Member, Scientific Advisory Board, Division of John Hopkins in Singapore

**Professional Societies:**

1983- American Association for the Advancement of Science, Member  
1986- American Association for Cancer Research  
1988- Massachusetts Medical Society, Member  
1988- American Society for Clinical Oncology, Member  
1989- American College of Physicians, Member  
1990- American Society of Hematology, Member  
1992- American Society of Microbiology, Member  
1992- International Society of Experimental Hematology, Member  
1996- American Society for Clinical Investigation, Member  
1997- American Society of Gene Therapy, Member  
1998- Harvard Medical School, Program in Immunology, Member  
2002- Association of American Physicians, Member  
2003- International Society for Stem Cell Research, Member

**Community Service Related to Professional Work:**

1983- Pre-medical Advisor Committee, Senior Common Room Member, Dudley House, Harvard College  
1995- Biology Mentor Program, Weston High School  
2003- Scholars in Clinical Science Program, Harvard Medical School  
2005- Member, Dept. of Surgery Research Council Junior Faculty Mentoring Program  
2005- Mentor, Health Sciences and Technology Division, Harvard and MIT, MD/MEMP students

**Editorial Boards:**

1992- New England Journal of Medicine, Ad hoc reviewer  
1992- Journal of Clinical Oncology, Ad hoc reviewer  
1993- AIDS, Member  
1993-1995 Cytokines in Hematology/Oncology, Member  
1993- American Journal of Hematology, Ad hoc reviewer  
1993- Cancer, Ad hoc reviewer  
1993- Blood, Ad hoc reviewer  
1993- Experimental Hematology, Ad hoc reviewer  
1994- Science, Ad hoc reviewer  
1994- Proceedings National Academy of Sciences, U.S.A., Ad hoc reviewer  
1995- Nature Medicine, Ad hoc reviewer  
1995- Journal of Virology, Ad hoc reviewer  
1995- Journal of Acquired Immunodeficiency Disease, Ad hoc reviewer  
1997- Human Gene Therapy, Ad hoc reviewer

1997	Gene Therapy, Ad hoc reviewer
1998-	Nature Biotechnology, Ad hoc reviewer
1998-	Journal of Clinical Investigation, Ad hoc reviewer
1998-	AIDS Research and Human Retrovirus, Ad hoc reviewer
1999-	Cancer Gene Therapy, Ad hoc reviewer
2002-	Molecular and Cell Biology, Ad hoc reviewer
2002-	Leukemia, Ad hoc reviewer
2001-	Journal of Immunology, Ad hoc reviewer
2002-	Journal of Leukocyte Biology, Ad hoc reviewer
2003-	Stem Cells, Editorial Board Member
2003-	Experimental Hematology, Editorial Board Member
2003-	Blood, Associate Editor
2004-	Immunity, Ad hoc reviewer
2004-	Nature Immunology, Ad hoc reviewer
2004-	Genes and Development, Ad hoc reviewer
2004-	Development, Ad hoc reviewer
2004-	Journal of Cell Biology, Ad hoc reviewer
2004-	Nature Cell Biology, Ad hoc reviewer
2005-	Journal of Stem Cells, Editorial Board member

#### **Awards and Honors:**

1973	Phi Alpha Theta, International History Honor Society, Bucknell University
1975	B.A. Cum Laude with Honors in English Literature, Bucknell University
1979	Alpha Omega Alpha, National Honor Medical Society, Case Western Reserve School of Medicine
1980	Edwin C. Garvin, M.D., Senior Prize, Case Western Reserve School of Medicine
1988	Physician Scientist Award, National Institutes of Health
1995	Saltonstall Scholar of Medicine, Massachusetts General Hospital, Harvard Medical School
1996	American Society of Clinical Investigation, elected
2001	Doris Duke Innovation in Clinical Research Award
2001	Honorary Consultant, Chinese Foundation for the Prevention of STD and AIDS
2002	Burroughs Wellcome Fund Clinical Scientist in Translational Research Award
2002	Association of American Physicians, elected
2002	Honorary Professor, Institute of Hematology, Peking Union Medical College, Chinese Academy of Medical Sciences
2002	Interurban Clinical Club, elected
2002	Alan Goldfine Leadership Chair of Research, Brain Tumor Society
2004	Leukemia and Lymphoma Society, Translational Research Award

## **PART II. Research, Teaching and Clinical Contributions**

### **A. Narrative Report:**

I started my research career focusing on retroviruses as a pathogenic model for hematologic disease as a post-doctoral fellow in the Howard Hughes laboratory of Dr. James M. Cunningham. The AIDS

epidemic was then at full force and my research evolved into a focus on HIV. During the 1990s, I developed a program of patient care, clinical trials and basic investigation while at the then Deaconess Hospital and eventually at the MGH. The clinical research program has contributed a standard of care for advanced Kaposi's sarcoma (paclitaxel) (*J Clin Oncol*), played a role in studies that resulted in three new FDA approved therapies and engaged patients in trials that defined underlying immunologic and hematologic function in AIDS (*J Immunol, Blood*). My role in the field included national and international administrative activities such as Chairmanship of the NCI-sponsored AIDS Malignancy Consortium and involvement on NCI advisory panels and for international organizations.

AIDS complications in the U.S. have waned and my emphasis has moved from hematopoietic cells as viral targets to potential therapeutic tools. I decided that ultimately making a difference in AIDS involves rebuilding the immune system and have focused on doing so from the stem cell up. My lab has worked on the physiology of primitive cells in HIV infection and provided definitive molecular evidence that hematopoietic stem cells are sanctuary cells, uninfected by the virus (*Blood, J Virol*). This led to detailed molecular characterization of the stem cell (*Science*) and definition of gene expression changes as normal, primary human stem cells underwent lineage specific differentiation (*Proc Natl Acad Sci USA*). These studies were the platform for subsequent work on stem cell regulation.

We sought to address the question of what dictates the characteristic quiescence of stem cells? Using comparative gene expression analysis in functionally defined subsets of cells, we identified candidates and then subsequently defined that the cyclin dependent kinase inhibitor, p21<sup>cip1/waf1</sup>, serves as a critical molecular switch (*Science*). Absent this gene product, stem cells more rapidly cycle and are more abundant *in vivo*. In addition, without this molecule, stem cells deplete prematurely under conditions of stress leading to animal mortality. We therefore defined a molecular contributor to stem cell quiescence and provide evidence that quiescence is a physiologic imperative for longevity.

We then asked whether other cyclin dependent kinase inhibitors participate in stem cell regulation. We demonstrated that despite molecular similarities, p27<sup>kip1</sup> plays an entirely distinct role in hematopoiesis. We showed that p27<sup>kip1</sup> functions at the more mature progenitor level markedly affecting the size of that cell pool (*Nature Medicine*). These differentiation stage specific effects of p21<sup>cip1/waf1</sup> and p27<sup>kip1</sup> had not been previously recognized.

To address whether these mediators of cell cycle control were dictated by external factors, we assessed cell surface expressed candidate gene products. We defined that TGFβ influences cell cycling independent from either p21 or p27 (*Blood*). We showed however that Notch1 receptor activation enhanced self-renewal of stem cells *in vivo* and altered the balance of lymphoid and myeloid differentiation (*Blood*). We further defined a G protein-coupled receptor of the purine/pyrimidine receptor family (P2Y), GPR105, restricted in expression to quiescent hematopoietic stem cells and functioning in cell migration (*Genes and Development*). These studies provided evidence for Notch as a key mediator of stem cell function *in vivo* and identified a new class of receptors modulating the stem cell compartment. We reported a series of studies on stem and hematopoietic cell localization including mechanisms for chemokine receptor mediated mature cell egress from organs of differentiation (*Nature Medicine, J Clin Invest, Nature Biotechnol, J Immunol, Blood*). In addition, we developed techniques for the isolation (*Nature Biotechnol*), targeted T cell differentiation (*Nature Medicine, Nature Biotechnol*) and *in vivo* tracking of stem cells (*Nature Biotechnol*), each with potential clinical implications.

Stem cell regulation is largely dictated by events in the microenvironment, but the stem cell niche in vivo had not been defined. We reasoned that the bone marrow resided in bone due to a regulatory relationship of bone to hematopoiesis and demonstrated through an animal model that specific activation of osteoblasts increased the stem cell pool in vivo. We defined that this was mediated by Notch1 activation and could be recapitulated by osteoblast activation using parathyroid hormone. This manipulation could increase stem cell numbers in vivo, increase stem cells in ex vivo culture and provide substantial improvement in animal survival following bone marrow transplantation (*Nature*). These data provide definition of osteoblasts as part of the stem cell niche in vivo and show that manipulating the niche, rather than the stem cell directly, can influence stem cell outcomes. Further they provide a strategy for affecting stem cell based therapies, using an available drug, providing a ready avenue of translation into the clinic.

In sum, my activities in AIDS hematology/oncology generated at the height of the epidemic have now been modified to focus on hematopoietic stem cells. I am committed to creating a program where basic understanding of stem cell regulation can be put to practical use in clinical settings, particularly in the context of cancer and AIDS. In doing so, I believe we can foster the basis for bringing developmental biology to medicine, creating an environment in which laboratory and clinical investigators can train, find fertile opportunity for innovative ideas and use an existing infrastructure to put concepts into practice.

#### **B. Funding Information:**

- 02/88-02/91    National Institutes of Health: PI  
Physician Scientist Award, National Cancer Institute.
  
- 10/90-12/93    Sandoz: PI  
A Phase I, Open-label Trial of SDZ ILE 964 (RhIL-3) in AIDS Patients With Cytopenia.
  
- 11/90-10/94    Amgen: PI  
Consensus Interferon Alpha for AIDS-associated Kaposi's Sarcoma.
  
- 02/91-07/96    National Institutes of Health: RO1-HL44851/PI  
Mechanisms of Hematopoiesis in AIDS.
  
- 07/91-01/95    National Institutes of Health: RO1-CA55520/PI  
Biological Approaches to AIDS Lymphoma.
  
- 03/92-11/95    Genentech: Co-PI  
Exploratory Studies on Hematopoiesis and Megakaryocytopoiesis.
  
- 04/92-04/95    Immunex: PI  
Recombinant Human Granulocyte - Macrophage Colony Stimulating Factor ("rhuGm-CSF") to Modulate the Antiviral Efficacy of Zidovudine (AZT).

- 06/92-04/95 Immunogen: National PI  
Treatment of HIV-associated NHL Using Modified mBACOD Chemotherapy Plus the Immunoconjugate Anti-B4-blocked Ricin.
- 08/92-09/95 Vestar: PI  
DaunoXome vs. Combination Chemotherapy ABV for Kaposi's Sarcoma.
- 04/93-06/94 Hoffman-La Roche: PI  
A Phase II Study of Oral TAT Antagonist for AIDS-associated Kaposi's Sarcoma.
- 08/93-06/95 Amgen: PI  
Randomized, Controlled, Multicenter Trial of Filgrastim for Neutropenia in Patients with AIDS.
- 09/93-09/96 National Institutes of Health: RO3-CA62686/PI  
Immunoconjugate Therapy for Relapsed AIDS Lymphoma.
- 09/93-09/98 National Institutes of Health: RO3-CA62776/PI  
Adoptive Immunotherapy for AIDS Lymphoma.
- 01/94-09/95 Immunogen: National PI  
Anti-B4-blocked ricin plus CHOP chemotherapy for AIDS Lymphoma
- 01/94-10/95 ID Biomedical: PI  
Cycling Probe Reaction Evaluation for HIV-1.
- 07/94-06/95 AmFar - Co PI  
*In vitro* models of immune reconstitution in HIV.
- 08/94-04/98 National Institutes of Health, NIAID: RO1-A136550/Co-PI  
MGH/awarding institution, Immune Reconstitution in AIDS virus infection.
- 11/94-07/98 Ilex: PI  
MGBG for relapsed AIDS Lymphoma
- 12/94-11/95 Clark Foundation: PI  
*In vitro* models of gene therapy for AIDS.
- 08/95-07/00 National Institutes of Health: RO1-DK50234/PI  
Functional Isolation of Human Hematopoietic Stem Cells.
- 09/0/-08/06 National Institute Of Health: PO1-DE14388-03 (Wang)  
Oral T Cell Responses to EBV, KSHV and HIV
- 09/95-04/00 National Institutes of Health: RO1-HL55718/PI  
Comparative Biology of Hematopoietic Stem Cells.

09/95-07/04 National Institutes of Health: UO1-CA71375-09S1 (Scadden)  
Boston AIDS Malignancies Consortium.

02/96-04/97 Ligand: PI  
LGD 1057 for Kaposi's sarcoma, Phase I, II

04/96-04/98 Ligand: PI  
AR 1057 for Kaposi's sarcoma Phase III

8/96-07/01 National Institutes of Health: RO1-HL44851/PI  
Mechanisms of Hematopoiesis in AIDS.

09/96-07/02 National Institutes of Health: RO1-CA73580/PI  
Immunobiology of HHV-8 in Kaposi's sarcoma.

02/97-04/98 Baker-Norton: PI  
Paclitaxel for Kaposi's sarcoma

03/97-02/99 Cytran, Inc.:PI  
IM-862 product nasal solution open label protocol for evaluation of treatment in Kaposi's sarcoma.

04/97-03/01 Department of Defense, DARPA: 9624-FP-111/PI  
Immune Cell-based countermeasures to biologic pathogens and myelotoxins.

09/02-03/05 DAMD 17-02-C-0125337 (Craiu)  
DARPA (subcontract)  
Novel meyhods for stem cell isolation and stem cell fate decisions, in support of the ex Vivo immune system

05/97-04/99 Cell Genesys:PI  
Pilot study of autologous CD4-zeta gene-modified T cell infusion with or without IL-2 in patients with HIV infection.

05/97-04/99 Cell Genesys: PI  
Phase II study of autologous CD4-zeta gene-modified T cells with or without exogenous interleukin-2 in HIV-infected patients.

08/97-07/98 Bristol-Meyers Squibb:PI  
Paclitaxel for patients with AIDS-associated Kaposi's sarcoma

08/97-07/98 Immunex, Inc.:PI  
Phase III double blind placebo controlled trial of recombinant human GM-CSF in patients with advanced HIV disease

- 04/98-03/99 Cell Genesys: PI  
Phase II study of autologous CD4-zeta gene-modified T cells in HIV infected patients with undetectable plasma viremia on combination antiretroviral drug therapy.
- 07/98-06/02 National Institutes of Health: K12- CA77845-01/PI  
Boston AIDS Oncology Training Program.
- 07/98-05/01 National Institutes of Health: PO1-CA78378 (Anderson)  
Novel immune-based therapies for multiple myeloma.
- 10/98-11/99 SyStemix, Inc.: PI  
A Phase I/II study in HIV-1 infected patients infused with CD34++Thy+hematopoietic stem cells (HSC) from G-CSF mobilized peripheral blood retrovirally transduced with RevM10/antisense POLI.
- 10/98-11/99 SyStemix, Inc.: PI  
A Phase I/II study of the Safety & Feasibility of RevM10 transduced hematopoietic stem cells in HIV-related non-Hodgkin's lymphoma patients already being treated with high dose chemotherapy.
- 03/99-07/03 National Institutes of Health/SBIR/Co-PI  
Science Research Laboratory (MGH subcontract)  
Purging progenitor cell preparations by pulsed electric fields.
- 09/99-07/03 National Institutes of Health: U01 CA70019-05 (Lee)  
AMC Operations Center – Supplement
- 08/01-07/03 National Institutes of Health: U01 CA70019-07 (Lee)  
Chair of AMC Lymphoma Working Group
- 07/00-10/01 NASA/SBIR/Science Research Laboratory (Craiu)  
Microgravity Enhanced Biological Cell Selection
- 08/00-07/03 National Institutes of Health: U01 CA70019-07 (Lee)  
T Cell Responses to KSHV in Mother to Child Transmission
- 08/01-07/03 National Institutes of Health: U01 CA70019-07 (Lee)  
AMC supplement 14/ International Infrastructure
- 08/00-07/05 National Institutes of Health: P50 CA86355-04 (Weissleder)  
Center for Molecular Imaging Research
- 09/00-08/05 National Institutes of Health: P30 AI42851 (Walker)  
Partners/Fenway/Shattuck Center for AIDS Research
- 12/00-11/05 National Institutes of Health: P01 AI29530 (Ritz)

Modeling T-cell Neogenesis after Allogeneic Stem Cell Transplantation

- 02/01-01/06 National Institutes of Health: R01 HL65909-04 (Scadden)  
Targeted Manipulation of Stem Cells for AIDS Therapy
- 04/01-03/06 National Institutes of Health: R01 DK50234-07 (Scadden)  
Functional Isolation of hematopoietic stem cells
- 08/95-03/05 National Institutes of Health: R01 DK50234-10 (Scadden)  
Functional Isolation of Human Hematopoietic Stem Cells (Supplement)
- 07/01-06/04 Doris Duke Charitable Foundation: Innovation in Clinical Research Award  
Stem Cell Expansion Through Manipulation of p21Cip1
- 07/02-06/07 Burroughs Wellcome Fund: Clinical Scientist Award in Translational Research  
Developing Control Mechanism-Based Stem Cell Therapies
- 02/91-07/06 National Institutes of Health: RO1-HL44851-14/ (Scadden)  
Mechanisms of Hematopoiesis in AIDS.
- 01/04-12/04 The Foundation For A Cure For Mitochondrial Disease, Inc. (Scadden)  
Stem Cell Transplant Therapy for Treating Mitochondrial Disease
- 04/03-03/08 National Institute of Health: RO1-HL070866-02 (Jones)  
FIO2 and Blood Vessel Formation in Adult Lung
- 05/04-04/05 (Seiden) PI  
DFHCC/Howard Hughes Spores Subcontract Project 4
- 10/04-09/07 Leukeima and Lymphoma Society 6178-05 (Scadden)  
Therapeutic Manipulation of the stem cell niche
- 10/04-05/07 DARPA (subcontract) (Craiu)  
Ex-vivo Functional Bone Marrow and thymic Microenviroment

**C. Report of Current Research Activities**

Stem cell biology is the major focus of my current research effort. Specifically, the lab continues to emphasize cell cycle control with an emerging emphasis on understanding the interaction of stem cells with their microenvironment in affecting cell phenotype. We have systematically assessed how a series of cyclin dependent kinase inhibitors can influence the kinetics and pool size of the hematopoietic stem cells and shown that by knocking down expression of at least one such molecule (p21) stem cell expansion can proceed. We are collaboratively investigating the link between Notch1 activation and CDKIs defining a molecular pathway joining them to account for the synergistic effect on stem cell pools. Our interaction with tissue engineering expertise in the nascent Center for Regenerative Medicine



and Technology is particularly timely for the increasing emphasis on how stem cells are guided by their environment. To define how stem cell location in bone marrow may be affected by bone, we have established collaborative relationships with bone biologists. Through these interactions, we have tested genetic alterations of bone constituents and their impact on stem cells. These results have defined that the cellular, mineral and matrix constituents of bone alter the localization, proliferation or survival of hematopoietic stem cells. These studies are ongoing and provide the first defined elements of a microenvironmental niche in controlling the behavior of mammalian stem cells.

The clinical research emphasis of my program has decreased with the changes in the HIV epidemic, but I continue to remain active in the development and conduct of clinical studies in AIDS related malignancies. Specifically, I am the national chair on a multi-institutional bone marrow transplant study for relapsed AIDS lymphoma and a phase III trial for up-front therapy of AIDS lymphoma. I am involved in studies on Kaposi's sarcoma here in the U.S. and in South Africa and continue to provide input to understanding immunologic aspects of KSHV infection now guided by a former trainee. As stem cell based therapies are enabled by my laboratory effort, reconstituting HIV resistant immune function in AIDS is our planned target.

#### **D. Report of Teaching:**

##### **1. Local Contributions**

###### **a. Harvard Medical School Courses**

1988-1989	Introduction to Clinical Medicine Preceptor Two medical students/year, 10 hours prep/15 hours contact
1994	Hematology Pathophysiology (New Pathway HMS II) Tutor Eight medical students/year in tutorial Twenty students in section Three weeks/year, 12 hours prep /18 hours contact
1994	Hematology Pathophysiology (New Pathway HMS II) Section instructor Fifteen students per section Three weeks/year, 6 hours prep /9 hours contact
1995	Hematology Pathophysiology (New Pathway HMS II) Section instructor Fifteen students per section Three weeks /year, 6 hours prep /9 hours contact
1998	Design and Conduct of Clinical Trials Faculty member 25 Fellows

Six weeks/year, 2 hours prep /2 hours contact

c. Local invited teaching presentations:

- |              |                                                                                                                                                                                                                                                                                                                                                                                                                                           |
|--------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1988-present | Hematology Consult and In-patient Attending<br>Attending<br>One Fellow, 0-1 Resident, 0-1 Student<br>One month/year, 4 hours prep /25 hours contact                                                                                                                                                                                                                                                                                       |
| 1988-1992    | Oncology Consult and In-patient Attending<br>Attending<br>One Fellow, 0-1 Resident, 0-1 Student<br>One month/year, 4 hours prep/25 hours contact                                                                                                                                                                                                                                                                                          |
| 1989         | Medical Services Attending<br>Two Students, 3 Residents<br>One month, 6 hours prep/20 hours contact                                                                                                                                                                                                                                                                                                                                       |
| 1989         | Medical Grand Rounds Lecturer<br>Residents, Fellows, Staff/50 Attendees, 2 hours prep/1 hour contact                                                                                                                                                                                                                                                                                                                                      |
| 1993         | Grand Rounds<br>Two affiliated teaching hospitals: AIDS Hematology/Oncology<br>Tumor Board: Oncology teaching hospital, "AIDS malignancies."<br>Research Rounds: Two affiliated teaching hospitals, "Molecular studies of<br>hematopoiesis."<br>10-30 attendees, 4 hours prep/4 hours contact                                                                                                                                             |
| 1994         | Hematology/Oncology Grand Rounds: Longwood Medical Area Hospitals,<br>"AIDS-related malignancies."<br>80 attendees, 3 hours prep/1 hour contact<br><br>Invited Speaker: Newton Wellesley Hospital, "AIDS-related malignancies."<br>30 attendees, 1 hour prep/1 hour contact                                                                                                                                                               |
| 1995         | Medical Grand Rounds: Deaconess Hospital, "AIDS-related malignancies."<br>100 attendees, 3 hours prep/1 hour prep<br><br>Oncology Grand Rounds: New England Medical Center, "HIV-related<br>malignancies; management and epidemiology."<br>50 attendees, 1 hour prep/1 hour contact<br><br>Infectious Disease Grand Rounds: Massachusetts General Hospital, "AIDS-<br>related malignancies."<br>20 attendees, 2 hours prep/1 hour contact |

Medical Grand Rounds: Lahey Clinic, "Functional isolation and characterization of human hematopoietic stem cells."

20 attendees, 2 hours prep/1 hour contact

Medical Grand Rounds: Waltham/Weston Hospital, "AIDS-related malignancies."

20 attendees, 1 hour prep/1 hour contact

Transfusion Rounds: Brigham and Women's Hospital, "Functional isolation and characterization of human hematopoietic stem cells."

30 attendees, 1 hour prep/1 hour contact

Medical Grand Rounds: Cambridge Hospital, "AIDS malignancies overview and update."

25 attendees, 1 hour prep/1 hour contact

Invited Speaker: St. Elizabeth's Hospital, "The functional isolation and characterization of human hematopoietic stem cells."

30 attendees, 1 hour prep/1 hour contact

Invited Speaker: Fenway Community Health Center, "AIDS-related neoplasms."

30 attendees, 1 hour prep/1 hour contact

1996

Hematology/Oncology Research Medical Grand Rounds: Brigham and Women's Hospital/Beth Israel Hospital, "Recent developments in AIDS malignancies."

40 attendees, 1 hour prep/1 hour contact

Dermatology Grand Rounds: Harvard Medical School, "Kaposi's sarcoma."

50 attendees, 1 hour prep/1 hour contact

1997

Oncology Grand Rounds: Salem Hospital, "HIV-related malignancies."

25 attendees, 1 hour prep/1 hour contact

Grand Rounds: St. Vincent's Hospital, "Cytokines in HIV disease."

20 attendees, 1 hour prep/1 hour contact

Grand Rounds: Roswell Park Cancer Institute, "AIDS-related malignancies."

35 attendees, 1 hour prep/1 hour contact

Oncology Rounds: Salem Hospital, "HIV-related malignancies."

20 attendees, 1 hour prep/1 hour contact

Hematology/Oncology Grand Rounds: Columbia-Presbyterian Medical Center,

- “AIDS-related malignancies.”  
35 attendees, 1 hour prep/1 hour contact
- Transfusion Medicine Grand Rounds: Brigham & Women’s, “Case Discussion; Preliminary results of mononuclear cell collection.”  
20 attendees, 1 hour prep/1 hour contact
- 1998 Hematology/Oncology Grand Rounds: St. Elizabeth’s Medical Center, “AIDS-related malignancies.”  
30 attendees, 1 hour prep/1 hour contact
- Arthur Ashe Program in AIDS Care, Practice of AIDS Medicine course: Harvard AIDS Institute, Boston, MA. “AIDS Malignancies, Hematologic Complications and Immune Based Therapies.”  
25 attendees, 2 hours prep/1 hour contact
- Transfusion Medicine Grand Rounds: Brigham & Women’s Hospital, “Negative regulators of stem cells.”  
25 attendees, 2 hours prep/1 hour contact
- 1999 Arthur Ashe Program in AIDS Care, Practice of AIDS Medicine course: Harvard AIDS Institute, Boston, MA. “HIV-related Malignancies and Hematologic Complications.”  
25 attendees, 2 hours prep/1 hour contact
- 2000 Hematology/Oncology Grand Rounds: Pennsylvania Hospital, “Malignant complications of AIDS.”  
40 attendees, 2 hours prep/1 hour contact
- Dana-Farber/Partners Cancer Care Grand Rounds: Massachusetts General Hospital, “Making stem cells behave.”  
30 attendees, 2 hours prep/1 hour contact
- Harvard Medical School, Bone Marrow Transplant Grand Rounds: Dana-Farber Cancer Institute, “Designing rational strategies for stem cell manipulation.”  
50 attendees, 1 hour prep/1 hour contact
- Arthur Ashe Program in AIDS Care, The Practice of AIDS Medicine Course: Harvard AIDS Institute, Boston, MA. “HIV-related malignancies and hematologic complications.”  
25 attendees, 1 hour prep/1 hour contact
- Medical Grand Rounds: Massachusetts General Hospital, “Stem Cells: Forever Young?”  
60 attendees, 6 hours prep/1 hour contact

- Gastrointestinal Research Seminar Series: Massachusetts General Hospital, "Stem Cell Governance."  
20 attendees, 2 hours prep/1 hour contact
- 2001 New England Regional Primate Research Center Seminar Series, New England Regional Primate Research Center, Massachusetts, "Stem cells: designing rational strategies for manipulation."  
40 attendees, 2 hours prep/1 hour contact
- Invited Speaker: Chief's Conference, Cancer Center Seminars in Hematology and Oncology, Massachusetts General Hospital, Boston, MA. "Control Points in Stem Cell Proliferation and Differentiation."
- Immunology Seminar, Massachusetts General Hospital, "Stem cells: designing rational strategies for manipulation."  
50 attendees, 1 hour prep/1 hour contact
- Medical Grand Rounds, Lowell General Hospital, "Stem cells: what they do, why, how and where are we now?"  
50 attendees, 2 hours prep/1 hour contact
- Renal Unit Seminar, Massachusetts General Hospital, "Decision points in stem cell regulation." 50 attendees, 3 hours prep/1 hour contact
- Medical Services Attending  
1 month/year, 4 hours prep/48 hours contact  
2 Junior Residents, 1-4 Interns, 1-2 Students
- Harvard Medical School, Bone Marrow Transplant Rounds, Dana-Farber Cancer Institute. "Ex vivo strategies to encourage T cell regeneration."  
50 attendees, 2 hour prep/1 hour contact
- 2002 Dana-Farber/Partners CancerCare Grand Rounds: Massachusetts General Hospital, "Altering adult stem cell decision points to direct stem cell therapies"  
40 attendees, 2 hours prep/1 hour contact
- Medical Grand Rounds: Massachusetts General Hospital, "Immune Regeneration after Cancer or AIDS Therapy." 60 attendees, 6 hours prep/1 hour contact
- Harvard Immunology Program: Harvard Medical School, "Microenvironmental effects on Stem Cells." 100 attendees, 3 hours prep/2hour contact
- Center for Blood Research Seminar Series, Harvard Medical School: "Microenvironmental effects on primitive hematopoietic cells." 60 attendees, 2

hours prep/1 hour contact

2003

Hematology-Oncology Grand Rounds, Beth Israel Deaconess Medical Center, Boston, MA. "Can we make stem cells behave?" 30 attendees, 2 hours prep/1 hour contact time

Invited Speaker: Massachusetts General Hospital, Scientific Advisory Committee Meeting, Boston, MA. "Toward the rational manipulation of stem cells." 100 attendees, 3 hours prep/1 hour contact time

Hematology Division seminar series, Brigham and Women's Hospital.  
Invited speaker: "What bone does for bone marrow."  
30 attendees, 3 hours prep/1 hour contact time

BioMatrix Program, Harvard-MIT Division of Health Sciences and Technology: Stem Cell Research Panel participant. 60 attendees, 1 hour prep/2 hours contact time

Hematology/Oncology Program, Children's Hospital Medical Center, Dana Farber Cancer Institute/Harvard Cancer Center: "Defining and working the stem cell niche." 50 attendees, 3 hours prep/1 hour contact time

Center for Engineering in Medicine, Massachusetts General Hospital: "Microenvironmental Control of Stem Cells". 35 attendees, 2 hours prep/1 hour contact time

Cutaneous Biology Research Center, Massachusetts General Hospital, Boston, MA: "'Identifying and manipulating stem cell niche." 100 attendees, 1 hour prep/5 hours contact time

2004

Rheumatology Grand Rounds Dana Farber Cancer Center, Boston, MA. "Stem Cells" 80 attendees, 2 hours prep/1 ½ hours contact time

Rheumatology Grand Rounds, Massachusetts General Hospital, Boston, MA. "Stem Cells" 30 attendees, 2 hours prep/1 ½ hours contact time

Medical Grand Rounds, West Roxbury VA Medical Center, Boston, MA. "Stem cells: the basics and beyond" 100 attendees, 1 hour prep/1 hour contact

Invited panelist: Alumni/ae Day Symposium "The Ethical Complexities of Embryonic Stem Cell Research", Harvard Divinity School, Cambridge, MA. "Introducing the Harvard Stem Cell Institute."

Biomaterials and Tissue Engineering in Medical Devices and Artificial Organs Course (HST-521), Harvard-MIT Division of Health Sciences and Technology

Invited Speaker: "Cells for Tissue Engineering"

12 graduate student participants, 1 hour/2 hours contact time

Biomedical Engineering Seminar Series: Innovation in Biomedical Engineering and Biomedical Sciences, Harvard-MIT Division of Health Sciences and Technology

Invited Speaker: "Harnessing the body's endogenous potential for tissue regeneration by stem cells"

50 graduate student participants, 1 hour prep/1 hour contact time

2005

Tools of Human Investigation course, MGH Department of Medicine

Invited lecturer: "Stem Cell Research"

? residents, ? hours prep/1 1/2 hours contact time

d. Continuing Medical Education:

1993

Intensive Review of Oncology, Harvard Medical School

Lecturer: "AIDS-related neoplasms."

350 participants, 3 hours prep/1 hour contact

Intensive Review of Hematology and Hematologic Oncology, Harvard Medical School

Invited Speaker: "HIV infection: hematologic manifestations."

75 participants, 3 hours prep/1 hour contact

1996

AIDS Medicine: An Intensive Course, Harvard Medical School

Invited Speaker: "AIDS malignancies."

350 participants, 3 hours prep/1 hour contact

Infectious Diseases of Adults Postgraduate Course, Massachusetts General Hospital

Invited Speaker: "AIDS-associated malignancies."

350 participants, 2 hours prep/1 hour contact

1998

AIDS Medicine: An Intensive Course, Harvard Medical School

Invited Speaker: "AIDS malignancies."

350 participants, 3 hours prep/1 hour contact

AIDS-associated Malignancies: Biology and Clinical Management, University of California, San Francisco

Invited Speaker: "Hematologic complications of and approaches to HIV Disease."

2 hours prep/1 hour contact

1999

Pharmacy Continuing Education Program, Massachusetts College of Pharmacy and Health Sciences

Invited Speaker: "Erythropoietin in cancer and AIDS."

12 participants, 2 hours prep/1 hour contact

HIV, Cancer and Skin Disorders Conference, New England AIDS Education and Training Center

Invited Speaker: "HIV-related cancers."

35 participants, 2 hours prep/1 hour contact

Cancer Medicine and Hematology Postgraduate Course, Harvard Medical School

Invited Speaker: "Hematologic and neoplastic aspects of HIV infection."

450 participants, 2 hours prep/1 hour contact

AIDS Medicine: An Intensive Course, Harvard Medical School

Invited Speaker: "AIDS Oncology."

75 participants, 1 hour prep/1 hour contact

2000

AIDS-associated Malignancies: Biology and Clinical Management, University of California, San Francisco

Invited Speaker: "Adoptive cell transfer in the treatment of HIV and HIV-lymphoma."

2 hours prep/1 hour contact

Cancer Medicine and Hematology Postgraduate Course, Harvard Medical School

Invited Speaker: "Hematologic and neoplastic aspects of HIV infection."

350 participants, 2 hours prep/1 hour contact

AIDS Medicine: An Intensive Course, Harvard Medical School

Invited Speaker: "AIDS Oncology."

75 participants, 1 hour prep/1 hour contact

2001

Cancer Medicine and Hematology Postgraduate Course, Harvard Medical School

Invited Speaker: "Hematologic and neoplastic aspects of HIV infection."

350 participants, 2 hours prep/1 hour contact

AIDS Medicine: An Intensive Course, Harvard Medical School

Invited Speaker: "AIDS Oncology."

75 participants, 1 hour prep/1 hour contact



- 2002 Cancer Medicine and Hematology Postgraduate Course, Harvard Medical School  
Invited Speaker: "Hematologic and neoplastic aspects of HIV infection."  
350 participants, 3 hours prep/1 hour contact
- 2003 Current Progress in Tissue Engineering Review Course, Harvard Medical School  
Invited Speaker: "Stem cell interactions with their microenvironment or what bone does for bone marrow." 100 participants, 3 hours prep/1 hour contact time
- Cancer Medicine and Hematology Postgraduate Course, Harvard Medical School  
Invited Speaker: "Hematologic and Neoplastic Aspects of HIV Infection."  
150 participants, 4 hours prep/1 hour contact time
- 2004 Cancer Medicine and Hematology Postgraduate Course, Harvard Medical School  
Afternoon Session Chair. 150 participants, 4 hours prep/1 hour contact time

e. Advisory and Supervisory Responsibilities

- 1983 Harvard College Advisor: Co-chair, Dudley House Committee: Member, 5-10 students/year, 2 hour contact/3 hour prep time each/Advising
- 1986-present Harvard College Dudley House Committee: Member, 1-2 students/year
- 1990-1992 Harvard University AIDS Institute 1 post-doctoral fellow per year/150 hours/year: Supervisor/Mentor
- 1991 Harvard University AIDS Institute post-doctoral fellow: 100 hours/year: Advisor/Mentor
- 1990-present Post-doctoral research fellow: Supervisor, 1-10 scientists/year, 100 hours/year
- 2000-present Harvard University, Division of Medical Sciences: graduate student supervisor, 1 student/year/100 hours/year
- 2002-present Oxford University, U.K.: graduate student co-supervisor, 1 student/year/100 hours/year
- 2003-present Harvard College, Molecular and Cellular Biology: undergraduate student supervisor, 1 student/year/50 hours/year
- 2003-present Harvard Medical School Scholars in Clinical Science Program mentor: postdoctoral student advisor, 1 student/year/? hours per year

- 2003-present Harvard-MIT Division of Health Sciences and Technology HST 160 Clinical Mentor Program: clinical mentor for medical student, 1 student/year/10 hours per year
- 2004-present Harvard-MIT Division of Health Sciences and Technology: graduate student supervisor, 1 student/year/20 hours per year
- 2004-present Bucknell University Externship Program: undergraduate student mentor, 1 student/year/2 days per year

f. Advisees and Trainees

Duration of Training	Name	Current Position
1999-Present	Adams, Gregor, Ph.D.	Postdoctoral Fellow, Massachusetts General Hospital
2001-Present	Attar, Eyal, M.D.	Postdoctoral Fellow, Massachusetts General Hospital
2000-Present	Cohen, Kenneth, M.D.	Postdoctoral Fellow, Massachusetts General Hospital
2003-Present	Heather Fleming, Ph.D.	Postdoctoral Fellow, Massachusetts General Hospital
2003-Present	Haspel, Richard, M.D., Ph.D.	Postdoctoral Fellow, Massachusetts General Hospital
2003-Present	Janzen, Viktor, M.D.	Postdoctoral Fellow, Massachusetts General Hospital
2004-Present	Mukherjee, Siddhartha, M.D., Ph.D.	Postdoctoral Fellow, Massachusetts General Hospital
2002-Present	Orford, Keith, M.D., Ph.D.	Postdoctoral Fellow, Massachusetts General Hospital
2001-Present	Suscovich, Todd	Graduate student, Harvard University
1999-Present	Saito, Yoriko, M.D.	Postdoctoral Fellow, Massachusetts General Hospital
2003-2004	Sipkins, Dorothy, M.D., Ph.D.	Postdoctoral Fellow, Massachusetts General Hospital
1998-Present	Wang, Zhengyu, Ph.D.	Postdoctoral Fellow, Massachusetts General Hospital
2002-Present	Zhang, JieLin, M.D.	Visting scientist, BethIsrael Deaconess Hospital
1992-1994	Berardi, Anna, Ph.D.	Research Scientist, Institute Gustave Roussy
1997-2000	Brander, Christian, Ph.D.	Assistant Professor, Harvard Medical School
1995-2001	Carlesso, Nadia, Ph.D., M.D.	Assistant Professor, Harvard Medical School
1994-2000	Cheng, Tao, M.D.	Director, Stem Cell Biology,

1993-1995	Columbyova, Lucia, M.D.	Asst. Professor, U of Pittsburgh
1996-1997	Daga, Antonio, M.D., Ph.D.	Clinical practice
1998-2000	Evans, Richard, M.D.	Assistant in Medicine,
1992-1994	Feder, David, M.D.	University of Genoa, Italy
2001-2004	Forkert, Randolph, M.D.	Lecturer, University of Wales
1993-1995	Franken, Michael, M.D.	Res Fellow, McGill Univ. (now deceased)
2001-2003	Gallazi, Anna, M.D.	4th year resident, Medizinische Universitaetsspoliklinik Bonn, Germany
1996-1998	Gardner, Jason, Ph.D.	Section Director, Genzyme Corporation
1996-1997	Ishiyama, Taijiro, M.D.	Research Fellow, Mass. General Hospital
2003-2004	Lin, Chou-Wen, Ph.D.	Sr. Scientist, Chiron Pharmaceuticals
1998-2000	Miura, Nobuyuki, M.D., Ph.D.	Asst. Prof., Showa Univ. Sch. Of Med., Japan
1999-2000	O'Connor, Paula, M.D.	Asst. Prof., Pediatrics, Saitama Medical School, Japan
2001-2003	Patel, Dipti, M.D.	Program Leader, Genentech
2001-2004	Robertson, Paul, M.R.C.P.	Northern Virginia Oncology Associates
2001-2003	Rodrigues, Neil	Senior SHO in Infectious Diseases, Gartnavel Hospital, Edinburgh
1999-2000	Sarmiento, Leonor, B.S.	Graduate student, Oxford University, UK
1994-1999	Shen, Hongmei, Ph.D.	Graduate Student, University of Lisboa, Portugal
1999-2001	Stier, Sebastian, M.D.	Assistant Professor, University of Pittsburgh
2000-2002	Szczepiorkowski, Zbigniew, M.D., Ph.D.	Clinical trainee, University of Bonn, Germany
1998-2000	Whelan, John Patrick, M.D., Ph.D.	Assistant Professor, Dartmouth Medical School
1989-1990	Woon, Annie, M.D.	Instructor, Harvard Medical School
		Instructor, Harvard Medical School

## 2. Regional, National or International Contributions

### a. Invited presentations

- 1989      Invited speaker: American Red Cross XXth Annual Scientific Symposium. Hematopoietic Growth Factors in Transfusion Medicine. "GM-CSF in AIDS."
- Invited speaker: Immunotoxicology Discussion Group Spring Conference on Safety Assessment of Cytokines. "GM-CSF in AIDS."
- Invited speaker: American College of Physicians - University of Connecticut Symposium. "What's New in Internal Medicine. Hematopoietic Growth Factors."
- 1990      Invited speaker: 15th International Cancer Congress. Satellite Symposium on Cytokines in Tumor Therapy. "GM-CSF/Interferon/AZT for AIDS-associated Kaposi's Sarcoma."
- Invited speaker: American Cancer Society. 22nd Annual Medical Symposium. "AIDS related Neoplasms."
- Invited speaker: Medical College of Virginia Hematopoietic Growth Factor Symposium. "Applications of Growth Factors in the Treatment of AIDS."
- 1991      Invited plenary session speaker: International Society for Experimental Hematology. Parma, Italy. "Hematopoietic Abnormalities Associated with AIDS."
- Invited speaker: New York Medical College Symposium on Cytokines. "Growth Factors in AIDS."
- Invited speaker: Annual Meeting, New England Cancer Society. "AIDS Lymphoma and Kaposi's Sarcoma."
- Invited speaker: Community Research Initiative of New England. "Colony Stimulating Factors: G-CSF, EPO, and Others in AIDS."
- Invited speaker: Seventh Annual Review of Infectious Diseases for the Specialist. Rose Medical Center, Denver, CO. "Cytokines in AIDS."
- 1992      Invited speaker: International Conference on Growth Factors in Cancer Therapy. Nashville, TN. "Cytokines in AIDS."
- Invited speaker: American Cancer Society, Brigham and Women's Hospital: William C. Maloney Symposium on Advances in Clinical Hematology. "Hematologic Aspects of HIV disease."
- Invited speaker: Advances in Transfusion Medicine and Immunohematology Course: Yale University and Harvard University. "Biologic Therapies in

AIDS."

Invited speaker: Hartford Hospital AIDS Program Symposium. "AIDS-related Malignancies."

1993      Invited speaker: 3rd International Symposium on Cytokines in Hematology, Oncology and Immunology Satellite Symposium. Hannover, Germany. "Growth Factors in AIDS."

Invited speaker: Academy of Clinical Laboratory Physicians and Scientists. 28th Annual meeting. New Haven, CT. "Hematopoietic Abnormalities in AIDS."

Invited speaker: Tufts University. Symposium on Clinical Applications of Biologic Agents and Growth Factors in Cancer Therapy. "Cytokines in AIDS."

Invited speaker: Henry Ford Hospital. Hematology Malignancy Symposium. "AIDS-associated Malignancies."

1994      Invited speaker: Memorial Sloane-Kettering Cancer Center, New York, NY. "Isolation and Characterization of Quiescent, Multipotent Hematopoietic Progenitor Cells."

Invited speaker: 5th Bicon: Biennial Conference on Chemotherapy of Infectious Diseases and Malignancies, Salzburg, Austria. "Hematopoietic Growth Factors in the Treatment of HIV-infections."

Invited speaker: University of Indiana, Wells Center for Pediatric Research. Indianapolis, IN. "Isolation and Characterization of Quiescent, Multipotent Hematopoietic Progenitor Cells."

Invited speaker: Harvard Medical School New England Dermatological Society. Boston, MA. "Liposomal Daunorubicin for Kaposi's Sarcoma."

Invited Speaker: 2nd International Conference on Growth Factors in Hematology and Oncology. Atlanta, GA. "Growth Factors in AIDS."

Invited Speaker: Immunex Regional Meetings, Indianapolis, IN. "Cytokines in the Management of HIV Disease."

Invited Speaker: University of Southern California School of Medicine. Los Angeles, CA. "Effect of HIV on Bone Marrow Function".

Invited Speaker: The Institute for Medical Studies; Teleconference. "Cytokines in the Treatment of AIDS."

- 1995
- Invited Speaker: New York University Medical Center, New York, NY  
"Functional Isolation and Characterization of Stem Cells."
- Invited Speaker: 3rd International Conference Clinical Application of  
Cytokines and Growth Factors in Hematology/Oncology. Atlanta, GA. "Use  
of Growth Factors for AIDS."
- Invited Speaker: 4th International Symposium on Immunotoxins. "Combined  
Immunotoxin and Chemotherapy for initial treatment of AIDS lymphoma."  
Hollings Cancer Center, South Carolina.
- Invited Speaker: Chiron Corporation, San Francisco, CA. "Functional Isolation  
and Characterization of Stem Cells."
- Invited Speaker: University of Pennsylvania Medical Center, Institute for  
Human Gene Therapy.
- Invited Speaker: Walter Reed Army Institute of Research, Division of  
Retrovirology. Rockville, MD. "Functional Isolation and Characterization of  
Human Hematopoietic Stem Cells."
- Invited Speaker: Fanconi Anemia Annual Scientific Symposium. Boston, MA.  
"Novel methods of Isolating Stem Cells."
- Roundtable Symposium Invited Speaker: 2nd National Conference. Human  
Retroviruses and Related Infections. The American Society for Microbiology.  
Washington, DC. "Immune Reconstitution."
- Invited Speaker: Project Inform. Immune Restoration Think Tank: The  
Dobson Project. Houston, Texas.
- Invited Speaker: LAPAF and Immunex Corporation. Los Angeles, CA.  
"Developing HIV therapies from a Hematologist's view."
- Invited Speaker: AIDS Provider Group. Los Angeles, CA. "Cytokines in HIV  
disease."
- 1996
- Chair: International Symposium on Immunodeficiency and its relation to  
lymphoid and other malignancies. Berlin, Germany. "HIV- associated  
malignant lymphomas."
- Invited Speaker: University of Massachusetts Medical Center, Worcester, MA.  
"Mapping Gene Expression During Differentiation of Individual Hematopoietic  
Cells."
- Invited Speaker: Boston University School of Medicine, Whitaker

Cardiovascular Institute, Boston, MA. "Modeling lineage commitment in human hematopoietic cells."

Invited Speaker: The Third Conference on Retroviruses and Opportunistic Infections. Dallas, TX. ProMedica

Invited Speaker: Lindsley F. Kimball Research Institute, New York Blood Center, New York, NY. "Modeling lineage commitment in human hematopoietic cells."

Invited Speaker: International Workshop, Gene Targeting in Hematology/Oncology. Genova, Italy. "Modeling stem cell gene therapy for AIDS."

Invited Speaker: Sylvester Comprehensive Cancer Center, University of Miami, Florida. "AIDS-related malignancies."

Invited Speaker: Boston Users Group for Cytometry, "Function-based stem cell isolation."

Invited Speaker: Wayne State University/Harper Hospital, Detroit, MI. "Treatment of Kaposi's Sarcoma: Future Directions."

Invited Speaker: Martin Memorial Medical Center, Stuart, FL. "AIDS-related malignancies."

1997      Invited Speaker: The Center for Blood Research, Boston, MA.  
"Characterization of human hematopoietic stem cells."

Roundtable discussion: Sequus Pharmaceuticals, Inc. New York, NY. "Case Studies in Kaposi's Sarcoma: A Multidisciplinary Approach to Treatment."

Program Convener: 4th Conference on Retroviruses and Opportunistic Infections. Washington, DC. "Non-KS Malignancies: Bench to Bedside."

Invited Speaker: Current Issues and Future Directions in the Prevention of Invasive Fungal Infections. Los Angeles, CA. "Who is to benefit from cytokine therapy: Targeting patients at risk."

Invited Speaker: University of Alabama AIDS Research Center. Birmingham, AL. "AIDS-related lymphoma."

Invited Speaker: South Florida Oncology Review. Boca Raton, FL. "AIDS-related malignancies."

Invited Speaker: Massachusetts General Hospital, Boston, MA. Gastrointestinal

Unit Research Seminar. "Human hematopoietic stem cells."

Invited Speaker: Amgen, SCF/AIDS Preclinical Meeting, Westlake Village, CA. "SCF and the anemia, hematology, and immunology of AIDS."

Invited Speaker: Amgen, New Seabury, MA. "The clinical management of AIDS: antivirals, protease inhibitors and G-CSF Use."

Invited Speaker: 2<sup>nd</sup> Joint Conference NIAID SPIRAT/NCDDG-HIV programs, Vienna, VA. "New Opportunities for HIV therapy: From discovery to Clinical Proof-of-Concept."

1998      Invited Speaker: Indiana University, Indianapolis, IN. "Chemokine receptor function in hematopoietic stem cells."

Invited Speaker: Ortho Biotech, The Distinguished Faculty Program at Correctional Medical Service, Dedham MA "Hematologic aspects of HIV disease."

Invited Speaker: Massachusetts General Hospital, Boston, MA. Infectious Diseases of Adults Postgraduate Course. "AIDS-associated malignancies."

Invited Speaker: Ortho Biotech, The Distinguished Faculty Program. Shattuck Hospital, Boston, MA. "Hematologic aspects of HIV disease."

Invited Speaker: NIH/NHLBI, Bethesda, MD. "Negative regulators of hematopoietic stem cells."

Invited Speaker: Ortho Biotech, The Distinguished Faculty Program. Fenway Community Health Center, Boston, MA. "Hematologic aspects of HIV disease."

1999      Invited Speaker: Harvard AIDS Institute, International Symposium on HIV, Leukemia and Opportunistic Cancers, Marrakech, Morocco. "The Hematopoietic Stem as Target and Tool in HIV Disease."

Invited Speaker: Advanced Biotechnology Center, International Workshop, Verona, Italy. "Updates in Immunohematology and Oncology: From Cell Progenitors to Effector Functions."

2000      Invited Speaker: BIO 2000, 4<sup>th</sup> Annual Tech Transfer Forum, Boston, MA. "Novel Strategies for Modulating Immune Cell Localization".

Invited Speaker: Division of Hematology/Oncology Conference, University of Pennsylvania, Center for AIDS Research. "Defining Molecular Targets for Stem Cell Manipulation."



Roundtable Discussion Chair: 4<sup>th</sup> International AIDS Malignancy Conference, National Institutes of Health, Bethesda, MD. "New Directions in AIDS Lymphoma Treatment."

Invited Speaker: Hematology/Oncology Teaching and Research Seminar, New York University Medical Center. "Making Stem Cells Behave."

Invited Speaker: Institute of Human Virology Seminar, Virology Institute, Baltimore, MD. "Molecular targets for stem cell engineering."

Invited Speaker: Holland Laboratory Hematopoiesis Department Seminar, American Red Cross, Rockville, MD. "Molecular brakes on Stem Cell Proliferation."

Invited Speaker: 12<sup>th</sup> Annual International Fanconi Anemia Scientific Symposium, Amsterdam, The Netherlands. "The boundary between stem and progenitor cells is marked by distinct molecular regulators of cell cycle entry."

2001      Invited Speaker: UMASS Medical Center, Worcester, MA. "Stem cells: designing rational strategies for manipulation."

Invited Speaker: Ortho Biotech and Institute for Continuing Education Program, Living Longer, Living Stronger: Maintaining the Quality of Life for Patients with Anemia and HIV Infection. Fenway Community Health Center, Boston, MA "Hematological aspects of HIV Disease."

Indiana University School of Medicine Combined Seminar Series, Indiana University, Indiana, "Stem cells: designing rational strategies for manipulation."

Invited Speaker: Biology Department Seminar, Bucknell University, Lewisburg, PA. "Stem cell research."

Invited Speaker: HIV/AIDS Symposium, Immune Control of Paediatric and Adult HIV Infection in South Africa, Durban, South Africa. "AIDS-related malignancies."

Invited Speaker: Special Seminar, Genzyme Corporation, Framingham, MA. "Stem cells: designing rational strategies for manipulation."

Invited Speaker: Hematology Seminar Series, Department of Hematology, Yale University School of Medicine, New Haven, CT. "Designing rational strategies for stem cell manipulation."

Invited Speaker: Department of Cell Biology Seminar, Georgetown

University, Washington, DC. "Stem cells: designing rational strategies for manipulation."

Invited Speaker: National Center for AIDS Prevention and Control, Beijing, People's Republic of China. "Advances in understanding stem cells and their clinical implications."

Invited Speaker: Chinese Academy of Sciences, Beijing, People's Republic of China. "Strategies for achieving stem cell based therapies for AIDS."

Invited Speaker: Changhai Hospital, Shanghai Second Military Medical University, Shanghai, China. "Strategies for achieving stem cell based therapies for AIDS."

Invited Speaker: National Cancer Institute, Center for Cancer Research Grand Rounds, National Institutes of Health, Bethesda, MD. "Altering Adult stem cell decision points to direct stem cell therapies."

Invited Speaker: Department of Biomedical Research Division of Hematology and Oncology, Hematology/Oncology Grand Rounds, St. Elizabeth's Medical Center, Boston, MA. "Making stem cells behave."

2002      Invited Speaker: Hematology and Medical Oncology Grand Rounds, Memorial Sloan-Kettering Cancer Center, New York, NY. "Toward the rational manipulation of hematopoietic stem cells."

Invited Speaker: Division of Hematology-Oncology Seminar Series, Tufts University School of Medicine, New England Medical Center, Boston, MA. "Toward the rational manipulation of hematopoietic stem cells."

Invited Speaker: Department of Microbiology and Immunology Seminar Series, University of Montreal, Montreal, Canada. "Toward the rational manipulation of hematopoietic stem cells."

Invited Speaker: Dana-Farber/Partners Cancer Care Grand Rounds, Boston, MA. "Altering Adult Stem Cells Decision Points to Direct Stem Cell Therapies"

Invited Speaker: National Cancer Institute, Mouse Models of Human Cancers Consortium, Somatic and Embryonic Stem Cell Research Symposium, Bethesda, MD. "Molecular mediators of hematopoietic stem cell decision points."

Invited Speaker: The Children's Hospital of Philadelphia, Philadelphia, PA. "Toward the rational manipulation of hematopoietic stem cells."

Invited Speaker: MIT Lincoln Laboratory, New England Bioterrorism

Preparedness Workshop, Lincoln, MA. "Targeting Immunity to Biothreats Through Cell Manipulation."

Invited Speaker: Educational Meeting of the Physicians' Research Network, New York, NY. "Lymphoma in the Setting of HIV."

Invited Speaker: Basic Science Correlates Grand Rounds, Massachusetts General Hospital, Boston, MA. "Rebuilding Immunity after AIDS or Cancer Therapy."

Invited Speaker: Coriel Institute, University of Medicine and Dentistry of New Jersey, Camden, NJ. "Mechanisms governing hematopoietic stem cell localization."

Invited Speaker: Roger Williams Medical Center, Brown University, Providence, RI. "Altering Adult Stem Cell Decision Points to Direct Stem Cell Therapies."

Invited Speaker: American Society of Clinical Oncology Annual Meeting/Educational Symposia, Orlando, FL. "HIV-Related Cancers"

Invited Speaker: Institute of Human Virology, University of Maryland, "Stem cell regulatory mechanisms to guide gene therapy for AIDS."

Invited Speaker: Institute of Hematology, Chinese Academy of Medical Sciences, Tianjing, China. "Perspectives on Stem Cell Research"

Invited Speaker: Hematology/Oncology Research Seminar Series, University of Pennsylvania School of Medicine, Philadelphia, PA. "Location is everything: what the microenvironment does for stem cells."

Invited Speaker: Yale University School of Medicine, New Haven, CT "Toward the rational manipulation of stem cells."

Chair of panel: Dana-Farber Clinical Center Lymphoma and Viral Oncology Programs Minisymposium, Boston, MA. "Viral Pathogenesis of Lymphoma Malignancies."

Invited Speaker: International Meeting of the Institute of Human Virology, Baltimore, MD. "Developing Adult Stem Cell-Based Therapies"

Invited Speaker: Lund University, Lund, Sweden. "Influencing stem cell behavior: Cues from the microenvironment."

2003      Invited Speaker: Medicine Research Seminar Series, The University of Texas, San Antonio, TX. "Stem Cell Function and the Microenvironment Niche"

Invited Panel Speaker: Bioethical Issues Raised By the Mapping of the Human Genome Seminar, Academic Medical Development Company Meeting, Albany, NY. "Stem Cell Research: How Far Should We Go?"

Invited Speaker: Midwest Blood Club Symposium, Cincinnati, OH. "Toward the rational manipulation of stem cells."

Invited Speaker: CIMIT Center for Innovative Technology for Medicine, Boston, MA. "Making stem cells behave."

Invited Speaker: Biology Department Seminar, Bucknell University, Lewisburg, PA. "Stem cells: from biology to clinical use".

Invited Speaker: CIMIT Center for Innovative Technology for Medicine, Boston, MA. "Microenvironment Governing of Stem Cells".

Invited Speaker: American Association of Blood Banks Annual Meeting "Adult Stem Cells and their applications in regenerative medicine".

Invited Speaker: MD Anderson Cancer Center Blood and Marrow Transplantation Research Conference, Houston, TX. "Defining and manipulating the stem cell niche"

Invited Speaker: Dana-Farber/Partners Cancer Care Grand Rounds, Boston, MA. "Prospects for stem cell based therapies."

2004 Invited speaker: New York University, New York, NY. "Defining and manipulating the hematopoietic stem cell niche."

Invited speaker: University of Michigan, Department of Developmental Biology, "Defining and manipulating the hematopoietic stem cell niche."

Invited speaker: Institute of Hematology, Chinese Academy of Medical Sciences, International symposium on stem cells-Scientific, Medical, Societal, and Ethical aspects, Tianjing, China. "Defining and manipulating the stem cell niche".

Invited speaker: Asan-Harvard International Symposium IV, Seoul, Korea. "Defining and manipulating the stem cell niche" and "Mimicking in vivo microenvironments to manipulate stem cells ex vivo."

Plenary speaker: International Society for Stem Cell Research, Boston, MA. "Deconstructing the hematopoietic microenvironment."

Plenary speaker: International Society of Experimental Hematology, New Orleans, LA. "Defining and manipulating the hematopoietic stem cell niche." Also chair of concurrent session "Myeloproliferative Syndromes"

Keynote speaker: Kansas University Medical Center/Stowers Institute for Medical Research First Annual Kansas and Missouri Stem Cell Science Symposium, Kansas City, Missouri. "Normal and Leukemia Stem Cells and their Microenvironment"

Invited speaker: The VII International Meeting on In Utero Stem Cell Transplantation: New Frontiers in Regenerative Therapy, Rome, Italy. "Defining and manipulating the stem cell niche." Also chairman of session "Cord blood and adult stem cells"

Invited speaker: National Cancer Institute/Memorial Sloan-Kettering Cancer Center, 3<sup>rd</sup> Mouse Models of Hematopoietic Malignancies Workshop, New York, New York. "Defining and manipulating the stem cell niche."

Keynote speaker: Fourth Annual Meeting on Mesenchymal & Non-Hematopoietic Stem Cells: Focus on Adult Stem Cells, New Orleans, LA.

Invited speaker: The University of Texas/Southwestern Medical School, Dallas, TX. "Defining and manipulating the stem cell niche."

Keynote speaker: The American Society of Nephrology Renal Week, St. Louis, MO. "Regenerating Tissues and Organs: Fact or Fantasy?"

Invited speaker: The Leukemia & Lymphoma Society Stohlman Scholar Symposium, Denver, Colorado. "Therapeutic manipulation of the stem cell niche."

Plenary speaker: International Congress of the Cell Transplant Society, Boston, MA. "Hematopoietic stem cells and microenvironment."

Plenary speaker: 2<sup>nd</sup> Annual Australian National Stem Cell Centre National Conference, Sydney, Australia. "Defining and manipulating the hematopoietic stem cell niche."

Invited speaker: First International Stem Cell Symposium, Weizmann Institute of Science, Rehovot, Israel. "Therapeutic manipulation of the stem cell niche."

**b. Professional Leadership Roles Related to Teaching**

- |      |                                                                                                                         |
|------|-------------------------------------------------------------------------------------------------------------------------|
| 1991 | Educational Session on AIDS: American Society of Hematology Annual Meeting. "Hematologic dysfunction induced by HIV-1." |
| 1993 | Educational Session on AIDS, Chair, American Society of Hematology Annual                                               |

Meeting.

- 1994      Program Committee and Chairperson of Session: 30th Annual Meeting of the American Society of Clinical Oncology. "Novel Approaches to AIDS-related Cancers/Protection and Stimulation of Normal Tissues."
- Simultaneous Session Co-Chairman, American Society of Hematology Annual Meeting. "Retroviral Diseases."
- 1995      Simultaneous Session Moderator, American Society of Hematology Annual Meeting. "Retroviral Diseases."
- 1996-1997    Program Committee: 1<sup>st</sup> International AIDS Malignancy Conference.
- 1997      Session Organizer and Chair: 4th National Conference on Human Retroviruses and Related Infections. American Society of Microbiology.
- Session Chairperson: 1<sup>st</sup> International AIDS Malignancy Conference.
- 1997-1998    Program Committee and Section Chair: 34th Annual Meeting of the American Society of Clinical Oncology.
- 1998      Program Committee and Section Chair: 40<sup>th</sup> American Society of Hematology Annual Meeting.
- Program Committee: 2<sup>nd</sup> International AIDS Malignancy Conference.
- Session Chairperson: 2<sup>nd</sup> International AIDS Malignancy Conference.
- 2<sup>nd</sup> International AIDS Malignancy Conference.
- 1999      Program Committee and Section Chair: 41<sup>st</sup> American Society Hematology Annual Meeting.
- Program Committee and Section Chair: 35<sup>th</sup> Annual Meeting of the American Society of Clinical Oncology.
- Program Committee: 3<sup>rd</sup> International AIDS Malignancy Conference.
- Session Moderator: Plenary Lecture, 3<sup>rd</sup> International AIDS Malignancy Conference.
- Program Committee: American Society of Microbiology Herpesvirus Meeting.
- 2000      Program Committee: 4<sup>th</sup> International AIDS Malignancy Conference.

Oral Session Moderator and Abstract Reviewer: "Immunodeficiency, Including HIV Infection." 42<sup>nd</sup> Annual Meeting of The American Society of Hematology, San Francisco, CA.

2001      Program Committee: 5<sup>th</sup> International AIDS Malignancy Conference

Roundtable Discussion Chair: 5<sup>th</sup> International AIDS Malignancy Conference, National Institutes of Health, Bethesda, MD. "Clinical Issues and New Directions in the Treatment of AIDS Malignancies."

Coordinating Scientific Reviewer: Immunodeficiency and HIV infection, 43<sup>rd</sup> Annual Meeting of the American Society of Hematology.

L'Association Francaise Contre Les Myopathies (AFM)/Harvard Medical School Steering Committee, Children's Hospital, Boston, MA. "Progress Towards Clinical Gene Therapy."

Invited Speaker, Education Program Session, *HIV*, 43<sup>rd</sup> Annual Meeting of The American Society of Hematology. "Stem cells in HIV infection."

Invited Speaker, Scientific Program Session, *Thymic Function and Efforts to Enhance Immunologic Recovery After Transplantation*, 43<sup>rd</sup> Annual Meeting of The American Society of Hematology. "Ex Vivo Differentiation on Three-Dimensional Matrices."

2002      Session Chair, 3<sup>rd</sup> Stem Cell Gene Therapy Conference, Rockville, MD. "Stem cell gene transfer biology."

Invited Speaker, Education Program Session, HIV-related cancers, 38<sup>th</sup> Annual Meeting of the American Society of Clinical Oncology. "AIDS-related lymphoma."

Session Chair and Invited Speaker, Institute for Human Virology International Meeting, Baltimore, Maryland. "Stem cell biology."

Abstract review committee, American Society of Hematology annual meeting

2003      Scientific Program Committee, International Society for Experimental Hematology annual meeting

Program Committee and Invited Speaker, 7<sup>th</sup> International AIDS Malignancy Conference, Bethesda, MD.

2004      Program Committee and Plenary Speaker, International Society for Stem Cell Research Annual Meeting, Boston, MA

Program Committee and Invited Speaker, 8<sup>th</sup> International AIDS Malignancy Conference, Bethesda, MD

Scientific Program Committee and Plenary Speaker, International Society for Experimental Hematology Annual Meeting, New Orleans, LA

Abstract review committee, American Society of Hematology annual meeting, San Diego, CA

### 3. Innovative educational programs

1998                      Clinical Applications of the Revised European-American Lymphoma Classification (R.E.A.L.). Through highly focused talks and discussion panels, comprised of pathologists and clinicians, this course is used as a teaching tool for clinicians on this new approach to lymphoma classification.

### E. Report of Clinical Activities

1. Hematology/Oncology, Massachusetts General Hospital and Dana-Farber Cancer Institute, 1 Outpatient Clinic/week; daily inpatient care
2. Patient Load
  - 3-15 patients/week
  - high level of care
3. Attending Physician, Hematology consult service, Massachusetts General Hospital (one month annually)



### **PART III: Bibliography**

#### **Original Articles**

1. Fineberg HV, Scadden DT, Goldman L. Care of patients with a low probability of acute myocardial infarction: Cost effectiveness of alternates to CCU admission. *N Engl J Med* 1984; 310:1301-1307.
2. Albritton L, Tseng L, Scadden D, Cunningham J. A putative murine ecotropic retrovirus receptor gene encodes a multiple membrane spanning protein and confers susceptibility to virus infection. *Cell* 1989; 57:659-66.
3. Molina JM, Scadden DT, Byrn R, Dinarello CA, Groopman JE. Production of tumor necrosis factor alpha and interleukin-1 beta by monocytic cells infected with human immunodeficiency virus. *J Clin Invest* 1989; 84:733-37.
4. Scadden DT, Fuller B, Cunningham JC. Human cells infected with retrovirus vectors acquire an endogenous murine provirus. *J Virol* 1990; 64:424-7.
5. Scadden DT. Granulocyte macrophage colony stimulating factor (GM-CSF) in AIDS. *Prog Clin Biol Res* 1990; 338:163-76
6. Molina JM, Scadden DT, Amirault C, Woon A, Vannier E, Dinarello CA, Groopman JE. Human immunodeficiency virus does not induce interleukin-1, interleukin-6 or tumor necrosis factor in mononuclear cells. *J Virol* 1990; 64:2901-2906.
7. Scadden DT, Zeira M, Woon A, Wang Z, Schieve L, Ikeuchi K, Lim B, Groopman JE. Human immunodeficiency virus infection of human bone marrow stromal fibroblasts. *Blood* 1990; 76:317-322.
8. Molina JM, Scadden DT\*, Sakaguchi M, Fuller B, Woon A, Groopman JE. Lack of evidence for infection of or effect on growth of hematopoietic progenitor cells after *in vivo* or *in vitro* exposure to human immunodeficiency virus. *Blood* 1990; 76:2476-2482. (\*Shared first author)
9. Scadden DT, Bering HA, Levine JD, Bresnahan J, Evans L, Epstein C, Groopman JE. Granulocyte-macrophage colony-stimulating factor mitigates the neutropenia of combined interferon alfa and zidovudine treatment of acquired immune deficiency syndrome-associated Kaposi's sarcoma. *J Clin Oncol* 1991; 9(5):802-8
10. Scadden DT, Bering HA, Levine JD, Bresnahan J, Evans L, Epstein C, Groopman JE. GM-CSF mitigates the neutropenia of combined interferon alpha and zidovudine treatment of AIDS-associated Kaposi's sarcoma. *J Clin Oncol* 1991; 9:802-808.
11. Scadden DT, Wang Z, Groopman JE. Quantitation of plasma human immunodeficiency virus type 1 RNA by competitive polymerase chain reaction. *J Infect Dis* 1992; 165(6):1119-23

12. Scadden DT, Wang Z, Groopman JE. Quantitation of plasma HIV-1 RNA by competitive polymerase chain reaction. *J Infect Dis* 1992; 165:1119-1123.
13. Avraham H, Scadden DT, Chi S, Broudy VC, Zsebo KM, Groopman JE. Interaction of human bone marrow fibroblasts with megakaryocytes: Role of the c-kit ligand. *Blood* 1992; 80:1679-1684.
14. Scadden DT, Agosti J. No antibodies to granulocyte macrophage colony-stimulating factor with prolonged use in AIDS. *AIDS* 1993; 7(3):438
15. Wang Z, Goldberg M, Scadden DT. HIV-1 suppresses erythropoietin production *in vitro*. *Exp Hematol* 1993; 21:683-688.
16. Freedman AR, Scadden DT. Viral activity in early HIV disease. *Curr Opin Hematol* 1994; 1(1):19-23
17. Lee J, Wang Z, Luoh S-M, Wood WI, Scadden DT. Cloning of *frk*, a novel human intracellular *src*-like tyrosine kinase-encoding gene. *Gene* 1994; 138:247-251.
18. Scadden DT, Wang A, Zsebo KM, Groopman JE. *In vitro* effects of stem-cell factor or interleukin-3 on myelosuppression associated with AIDS. *AIDS* 1994; 8:193-196.
19. Mark MR, Scadden DT, Wong ZY, Gu Q, Goddard A, Godowski PJ. *RSE*, a novel receptor-type tyrosine kinase with homology to *Axl/Ufo*, is expressed at high levels in the brain. *J Biol Chem* 1994; 269(14):10720-10728.
20. Avraham H, Banu N, Scadden DT, Abraham J, Groopman JE. Modulation of megakaryocytopoiesis by human basic fibroblast growth factor. *Blood* 1994; 83(8):2126-2132.
21. Bennett B, Wang Z, Kuang W-J, Wang A, Groopman JE, Goeddel DV, Scadden DT. Cloning and characterization of *HTK*, a novel transmembrane tyrosine kinase of the *EPH* subfamily. *J Biol Chem* 1994; 269:14211-14218.
22. Gallo KA, Mark MR, Scadden DT, Wang Z, Gu Q, Godowski PJ. Identification and characterization of *SPRK*, a novel *src*-homology domain-containing proline-rich kinase with serine/threonine kinase activity. *J Biol Chem* 1994; 269:15092-15100.
23. Price P, Johnson RP, Scadden DT, Jassoy C, Rosenthal T, Kalams S, and Walker BD. Cytotoxic CD8+ T lymphocytes reactive with Human Immunodeficiency Virus-1 produce granulocyte/macrophage colony-stimulating factor and variable amounts of interleukins 2,3 and 4 following stimulation with the cognate epitope. *Clin Immunol Immunopath* 1995; 74:100-106.
24. Berardi AC, Wang A, Levine JD, Lopez P, Scadden DT. Functional isolation and characterization of human hematopoietic stem cells. *Science* 1995; 267:104-108.

25. Scadden DT, Levine JD, Bresnahan J, Gere J, McGrath J, Wang Z, Resta DJ, Young D, Hammer SC. *In vivo* effects of interleukin-3 in HIV-1 infected patients with cytopenia. *AIDS Research and Human Retroviruses* 1995; 11:731-740.
26. Masood R, Zhang Y, Bond MW, Scadden DT, Moudgil T, Law RE, Kaplan MH, June B, Espina BM, Lunardi-Iskandar Y, Levine AM. IL-10 is an autocrine growth factor for AIDS-related B-cell lymphoma. *Blood* 1995; 12:3423-3430.
27. Columbyova L, Loda M, Scadden DT. Thrombopoietin receptor expression in human cancer cell lines and primary tissues. *Cancer Research* 1995; 55:3509-3512.
28. Berardi AC, Wang A, Abraham J, Scadden DT. Basic fibroblast growth factor mediates its effects on committed myeloid progenitors by direct action and has no effect on hematopoietic stem cells. *Blood* 1995; 86:2123-2129.
29. Freedman AR, Zhu H, Levine JD, Kalams S, Scadden DT. Generation of human T lymphocytes from bone marrow CD34+ cells in vitro. *Nature Medicine* 1996; 2:46-51.
30. Scadden DT, Pickus O, Hammer SM, Stretcher B, Bresnahan J, Gere J, McGrath J, Agosti JM. Lack of in vivo effect of granulocyte-macrophage colony-stimulating factor (GM-CSF) on human immunodeficiency virus-type 1 (HIV-1). *AIDS Res and Human Retroviruses* 1996; 12:1151-1159.
31. Gill P, Wernz J, Cohen P, Scadden DT, Mukwaya GW, Ross ME, et al. Randomized Phase III trial of liposomal daunorubicin (DaunoXome)<sup>TM</sup> versus Doxorubicin, Bleomycin, Vincristine (ABV) in AIDS-related Kaposi's sarcoma. *J Clin Oncol* 1996;14:2353-2364.
32. Cheng T, Shen H, Giokas D, Gere J, Tenen D, Scadden DT. Temporal mapping of gene expression levels during the differentiation of individual primary hematopoietic cells. *Proc Natl Acad Sci* 1996; 93:13158-13163.
33. Franken M, Estabrooks A, Cavacini L, Sherburne B, Wang F, Scadden DT. EBV-driven gene therapy for EBV-related lymphomas. *Nature Medicine* 1996; 2:1379-1382.
34. Rosenzweig M, Marks DF, Zhu H, Hempel, Mansfield K, Sehgal P, Kalams S, Scadden DT, Johnson P. In vitro T lymphopoiesis of human and rhesus CD34+ progenitor cells. *Blood* 1996; 87:4040-4045.
35. Levine AM, Tulpule A, Tessman D, Kaplan L, Giles F, Luskey BD, Scadden DT, Northfeld DW, Silverberg I, Wernz J, Espina B, VanHoff D. Mitoguazone therapy in patients with refractory or relapsed AIDS-related lymphoma: Results from a multicenter Phase II trial. *J Clin Onc* 1997;15:1094-1103.
36. Gardner JP, Zhu H, Colosi PC, Kurtzman GJ, Scadden DT. Robust but transient expression of AAV-transduced genes in human T-lymphopoiesis. *Blood* 1997; 90:4854-4864.

37. Radomska HS, Huettner CS, Cheng T, Scadden DT, Tenen DG. CCAAT/Enhancer binding protein  $\alpha$  is a regulatory switch sufficient for induction of granulocytic development from bipotential myeloid progenitors. *Mol Cell Biol* 1998; 18:4301-4314.
38. Wu CJ, Scadden DT. Posttransplant Kaposi's sarcoma treated with paclitaxel. *J Clin Oncol* 1998; 16(10):3478-9
39. Gardner JP, Rosenzweig M, Marks DF, Harper D, Gaynor K, Fallon RJ, Wall DA, Johnson RP, Scadden DT. T lymphopoietic capacity of cord blood-derived CD34+ progenitor cells. *Exp Hematol* 1998; 26:991-999.
40. Scadden DT, Schenkein DP, Bernstein Z, Luskey B, Doweiko J, Tulpule A, Levine A. Immunotoxin combined with chemotherapy for patients with AIDS-related non-Hodgkin's lymphoma. *Cancer* 1998; 83:2580-7.
41. Yamaguchi T, Olszak I, Chattopadhyay N, Butters RR, Kifor O, Scadden DT, Brown EM. Expression of extracellular calcium ( $\text{Ca}^{2+}$ )-sensing receptor in human peripheral blood monocytes. *Biochemical & Biophysical Research* 1998;246, 501-506.
42. Cabriaes S, Bresnahan J, Testa D, Espina BM, Scadden DT, Ross M, Gill PS. Extravasation of liposomal daunorubicin in patients with AIDS-associated Kaposi's sarcoma: a report of four cases. *Oncol Nurs Forum* 1998; 25(1):67-70
43. Jones D, Gulizia JM, Ballestras M, Kaye KM, Fletcher J, Winters GL, Scadden DT, Aster JC. Human herpesvirus 8-associated primary effusion lymphoma, plasmacytic infiltrates, and Kaposi's sarcoma in a HIV-negative cardiac transplant recipient. *N Engl J Med* 1998; 339:444-9.
44. Tulpule A, Yung RC, Wernz J, Espina BM, Myers A, Scadden DT, Cabriaes S, Ilaw M, Boswell W, Gill PS. Phase II trial of liposomal daunorubicin in the treatment of AIDS-related pulmonary Kaposi's sarcoma. *J Clin Oncol* 1998; 16:3369-74.
45. Shen H, Cheng T, Preffer FI, Dombkowski D, Tomasson MH, Golan DE, Yang O, Hofmann W, Sodroski JG, Luster AD, Scadden DT. Intrinsic human immunodeficiency virus type 1 resistance of hematopoietic stem cells despite coreceptor expression. *J Virol* 1999; 73: 728-37.
46. Schwartz JD, Howard W, Scadden DT. Potential interaction of antiretroviral therapy with paclitaxel in patients with AIDS-related Kaposi's sarcoma. *AIDS* 1999; 13(2):283-4
47. Nikolic B, Gardner JP, Scadden DT, Arn JS, Sachs DH, Sykes M. Normal development in porcine thymus grafts and specific tolerance of human T cells to porcine donor MHC. *J Immunol* 1999; 162:3402-7
48. Adams GB, McMullen M, Turner S, Olszak IT, Scadden DT, McClure MO, Poznansky MC. Isolation and transduction of CD34+ cells from small quantities of peripheral blood from HIV-1-infected patients not treated with hemopoietic growth factors. *J Acquir Immune Defic Syndr Hum Retrovirol* 1999; 21:1-8.

49. Carlesso N, Aster J, Sklar J, Scadden DT. Notch1-induced delay of human hematopoietic progenitor cell differentiation through altered cell cycle kinetics. *Blood* 1999; 93:838-48.
50. Gill PS, Tulpule A, Espina BM, Cabriaes S, Bresnahan J, Ilaw M, Louie S, Gustafson N, Brown M, Orcutt C, Winograd B, Scadden DT. Paclitaxel is safe and effective in the treatment of advanced AIDS-related Kaposi's sarcoma. *J Clin Oncol* 1999; 17:1876-1883.
51. Poznansky MC, La Vecchio J, Silva-Arietta S, Porter-Brooks J, Brody K, Olszak IT, Adams G, Ramstedt U, Marasco W, Scadden DT. Inhibition of HIV replication and growth advantage of CD4+ T-cells and monocytes derived from CD34+ cells transduced with an intracellular antibody directed against HIV-1 tat. *Human Gene Therapy* 1999; 10:2505-2514.
52. Turnbull JL, Patchen ML, Scadden DT. The polysaccharide, PGG-Glucan, enhances human myelopoiesis by direct action independent of and additive to early-acting cytokines. *Acta Haematol* 1999; 102:66-71.
53. Cavacini LA, Wisnewski A, Peterson JE, Montefiori D, Emes C, Duval M, Kingsbury G, Wang A, Scadden DT, Posner M. A human anti-HIV autoantibody enhances EBV transformation and HIV infection. *Clinical Immunology* 1999; 93:263-273.
54. Morgan MB, Goldstein NB, Scadden DT, Lacy J, Curiel DT, Curiel TJ. Treatment of EBV transformed tumors with antisense oligodeoxynucleotides against EBNA-1 enhances tumor chemosensitivity. *Tumor Targeting* 1999; 4:1-9.
55. Duvic M, Friedman-Kien AE, Looney DJ, Miles SA, Myskowski PL, Scadden DT, Von Roenn J, Galpin JE, Groopman J, Loewen G, Stevens V, Truglia JA, Yocum RC. Topical treatment of cutaneous lesions of AIDS-related Kaposi sarcoma using alitretinoin gel. *Arch Dermatol* 2000; 136:1461-69.
56. Tulpule A, Scadden DT, Espina BM, Cabriaes S, Howard W, Shea K, Gill PS. Results of a randomized study of IM862 nasal solution in the treatment of AIDS-related Kaposi's Sarcoma. *J Clin Oncol* 2000; 18:716-723.
57. Mitsuyasu RT, Anton PA, Deeks SG, Scadden DT, Connick E, Downs MT, Bakker A, Roberts MR, June CH, Jalali S, Lin AA, Pennathur-Das R, Hege KM. Prolonged survival and tissue trafficking following adoptive transfer of CD4 $\zeta$  gene-modified autologous CD4+ and CD8+ T cells in HIV-infected subjects. *Blood* 2000; 96:785-93.
58. Duvic M, Friedman-Kien AE, Looney DJ, Miles SA, Myskowski PL, Scadden DT, Von Roenn J, Galpin JE, Groopman J, Loewen G, Stevens V, Truglia JA, Yocum RC. Topical treatment of cutaneous lesions of acquired immunodeficiency syndrome-related Kaposi sarcoma using alitretinoin gel: results of phase 1 and 2 trials. *Arch Dermatol* 2000; 136(12):1461-9
59. Lewin M, Carlesso N, Tung C, Tang X, Cory D, Scadden DT, Weissleder R. HIV-tat derivatized magnetic nanoparticles allow in vivo tracking and recovery of hematopoietic progenitor cells. *Nature Biotechnology* 2000; 18:410-414.

60. Cheng T, Rodrigues N, Shen H, Yang Y, Dombkowski D, Sykes M, Scadden DT. Hematopoietic stem cell quiescence maintained by p21<sup>cip1</sup>/waf1. *Science* 2000; 287(5459):1804-8
61. Podesta M, Zocchi E, Pitto A, Cesare U, Franco L, Bruzzone S, Guida L, Bacigalupo A, Scadden DT, Walseth, TF, De Flora A, Daga A. Extracellular cyclic ADP-ribose increases intracellular free calcium concentration and stimulates proliferation of human hemopoietic progenitors. *FASEB* 2000; 14:680-690.
62. Olszak IT, Poznansky MP, Evans RH, Olson D, Kos C, Pollak MR, Brown EM, Scadden DT. Extracellular calcium elicits a chemokinetic response from monocytes in vitro and in vivo. *J Clin Invest* 2000; 105:1299-1305.
63. Poznansky MC, Olszak IT, Foxall R, Evans RH, Luster AD, Scadden DT. Active movement of T cells away from a chemokine. *Nature Medicine* 2000; 26:543-548.
64. Eppich H, Foxall R, Gaynor K, Dombkowski D, Cheng T, Silva-Arrieta S, Evans RH, Mangano J, Preffer FI, Scadden DT. Pulsed electric fields rapidly size-select hematopoietic cells and deplete tumor cell contaminants. *Nature Biotechnology* 2000; 18:882-7.
65. Poznansky MC, Evans RH, Foxall R Olszak IT, Piascik AH, Hartman KE, Brander C, Meyer TH, Pykett MJ, Chabner KT, Kalams SA, Rosenzweig M, Scadden DT. Efficient human T-cell generation using a thymic organoid on a biocompatible, inorganic grid. *Nature Biotechnology* 2000; 18:729-734.
66. Brander C, Suscovich T, Lee Y, Nguyen T, O'Connor P, Seebach J, Jones NG, van Gorder M, Walker BD, Scadden DT. Impaired CTL recognition of cells latently infected with Kaposi's sarcoma associated herpes virus (KSHV/HHV8). *J Immunol* 2000; 165:2077-83.
67. Cheng T, Rodrigues N, Dombkowski D, Stier S, Scadden DT. Stem cell repopulation efficiency, but not pool size is governed by p27<sup>kip1</sup>. *Nature Medicine* 2000; 6:1235-40.
68. Ellison LW, Carlesso N, Cheng T, Scadden DT, Haber DA. The Wilms tumor suppressor WT1 directs stage specific quiescence and differentiation of human hematopoietic progenitor cells. *EMBO* 2001; 20:1-13.
69. Ratner L, Lee J, Shenghui T, Redden D, Fayez H, Herndier B, Scadden DT, Kaplan L, Ambinder R, Levine A, Harrington W, Grochow L, Flexner C, Tan B, Straus D. Chemotherapy for HIV-associated non-Hodgkin's lymphoma in combination with highly active antiretroviral therapy. *J Clin Oncol* 2001; 19:2171-8.
70. Poznansky MC, Olszak IT, Foxall RB, Piascik A, Adams GB, Evans RH, Cheng T, Scadden DT. Tissue source dictates human fetal CD34+CD38- cell lineage outcome. *Exp Hematol* 2001; 29:766-74.

71. Shen H, Cheng T, Olszak I, Garcia-Zepeda E, Lu Z, Herrmann S, Fallon R, Luster AD, Scadden DT. CXCR-4 desensitization is associated with tissue localization of hematopoietic progenitor cells. *J Immunol* 2001; 166:5027-33.
72. Brander C, O'Connor P, Suscovich T, Jones NG, Kedes DH, Ganem DE, Martin JN, Osmond DH, Southwood S, Sette A, Walker BD, Scadden DT. Definition of an optimal CTL epitope in the latently expressed KSHV Kaposin protein. *J Inf Dis* 2001; 184:119-126.
73. Christmas P, Jones JP, Patten CJ, Rock D, Zheng Y, Cheng SM, Weber BM, Carlesso N, Scadden DT, Rettie AE, Soberman RJ. Alternative splicing determines the function of CYP4F3 by switching substrate specificity. *J Biol Chem* 2001; 276:38166-72.
74. Cheng T, Shen H, Rodrigues N, Stier S, Scadden DT. Transforming growth factor- $\beta$ 1 mediates cell cycle arrest of primitive hematopoietic cells independent of p21<sup>Cip1/Waf1</sup> or p27<sup>Kip1</sup>. *Blood* 2001; 98:3643-3649.
75. Cianfrocca M, Cooley TP, Lee JY, Rudek MA, Scadden DT, Ratner L, Pluda JM, Figg WD, Krown SE, Dezube BJ. Matrix metalloproteinase inhibitor COL-3 in the treatment of AIDS-related Kaposi's sarcoma: A phase I AIDS Malignancy Consortium study. *J Clin Oncol* 2002; 20:153-59.
76. Donato JL, Ko J, Kutok JL, Cheng T, Shirakawa T, Mao X-Q, Beach D, Scadden DT, Sayegh MH, Adra CN. Human HTm4 is a hematopoietic cell cycle regulator. *J Clin Invest* 2002; 109:51-58.
77. Miles SA, Dezube BJ, Lee JY, Krown SE, Fletcher MA, Saville MW, Kaplan L, Groopman J, Scadden DT, Cooley T, Von Roenn J, Friedman-Kien A. Antitumor activity of oral 9-cis-retinoic acid in HIV-associated Kaposi's sarcoma. *AIDS* 2002; 16:421-429.
78. Deeks SG, Wagner B, Anton PA, Mitsuyasu RT, Scadden DT, Huang C, Macken C, Richman DD, Christopherson C, June CH, Lazar R, Broad DF, Jalali S, Hege KM. A phase II randomized study of HIV-specific T-cell gene therapy in subjects with undetectable plasma viremia on combination anti-retroviral therapy. *Mol Ther* 2002; 5:788-97.
79. Stier S, Cheng T, Dombkowski D, Carlesso N, Scadden DT. Notch1 activation increases hematopoietic stem cell self-renewal in vivo and favors lymphoid over myeloid lineage outcome. *Blood* 2002; 99:2369-2378.
80. Poznansky MC, Olszak IT, Evans RH, Wang RH, Wang Z, Foxall RB, Olson DP, Weibrecht K, Luster AD, Scadden DT. Thymocyte emigration is mediated by active movement away from stroma derived factors. *J Clin Invest*. 2002; 109:1101-10.
81. Wang Z, Miura N, Bonelli A, Mole P, Carlesso N, Olson DP, Scadden, DT. Receptor tyrosine kinase, EphB4 (HTK), accelerates differentiation of select human hematopoietic cells. *Blood* 2002; 99:2740-2747.
82. Olson DP, Scadden DT, D'Aquila RT, De Pasquale MP. The protease inhibitor ritonavir inhibits the functional activity of the multidrug resistance related-protein 1 (MRP-1). *AIDS* 2002; 16:1-5.

83. Tulpule A, Groopman J, Saville MW, Harrington W Jr, Friedman-Kien A, Espina BM, Garces C, Mantelle L, Mettinger K, Scadden DT, Gill PS. Multicenter trial of low-dose paclitaxel in patients with advanced AIDS-related Kaposi sarcoma. *Cancer* 2002; 95:147-54.
84. Miles SA, Testa M, Huang J, Wade M, Carden J, Scadden DT. Lack of antitumor activity and intolerance of interleukin-4 in patients with advanced HIV disease and Kaposi's sarcoma. *J Interferon Cytokine Res.* 2002; 11:1143-8.
85. Cheng T, Scadden DT. Cell cycle entry of hematopoietic stem and progenitor cells by distinct cyclin-dependent kinase inhibitors. *Int J Hematol* 2002; 75:460-5.
86. Brander C, Raje N, O'Connor PG, Davies F, Davis J, Chauhan D, Hideshima T, Martin J, Osmond D, Kedes DH, Walker BD, Scadden DT, Anderson KC. Absence of biologically important Kaposi's sarcoma-associated herpesvirus gene products and virus-specific cellular immune responses in multiple myeloma. *Blood* 2002; 100:698-700.
87. Preffer FI, Dombkowski D, Sykes M, Scadden D, Yang Y-G. Lineage negative side population (SP) cells with restricted hematopoietic capacity circulate in human adult blood. *Stem Cells* 2002; 20:417-427.
88. Jiang Z, Adams GB, Hanash AM, Scadden DT, Levy RB. The contribution of cytotoxic and noncytotoxic function by donor T-cells that support engraftment after allogeneic bone marrow transplantation. *Biol Blood Marrow Transplant.* 2002; 8:588-96.
89. Anton P, Mitsuyasy R, Deeks S, Scadden DT, Wagner B, Huang C, Christopherson C, Akin J, et al. Multiple measures of HIV burden in blood and tissue are correlated with each other but not with clinical parameters in aviremic subjects. *AIDS* 2003; 17:53-63.
90. Adams GB, Chabner K, Foxall R, Rodriguez N, Dombkowski D, Fallon R, Poznansky MC, Scadden DT. Heterologous cells cooperate to augment stem cell migration, homing and engraftment. *Blood* 2003; 101:45-51.
91. Fukushima T, Miyazaki Y, Tsushima C, Taguchi J, Yoshida S, Kuriyama K, Scadden D, Nimer S, Tomonaga M. The level of MEF but not ELF-1 correlates with FAB subtype of acute myeloid leukemia and is low in good prognosis cases. *Leukemia Res.* 2003; 5:387-92.
92. Christmas P, Carlesso N, Shang H, Cheng S-M, Weber BM, Preffer FI, Scadden DT, and Soberman RJ. Myeloid expression of cytochrome P450 4F3 is determined by a lineage-specific alternative promoter. *J. Biol. Chem.* 2003; 278; 27; 25133-42.
93. Stier S, Cheng T, Forkert R, Lutz C, Dombkowski DM, Lin J, Scadden DT. Ex vivo targeting of p21<sup>Cip1/Waf1</sup> permits relative expansion of human hematopoietic stem cells. *Blood.* 2003; 102:1260-6.



94. Lee BC, Cheng T, Adams GB, Miura N, Lee SB, Attar EC, Saito Y, Olszak I, Dombkowski D, Olson DP, Hancock J, Haber DA, Luster AD, Scadden DT. P2Y-like receptor, GPR105, identifies and mediates chemotaxis of bone marrow restricted primitive hematopoietic cells. *Genes and Development*. 2003;17:1592-1604.
95. Calvi LM, Adams GB, Weibrecht KW, Weber JM, Olson DP, Knight MC, Martin RP, Schipani E, Bringham FR, Divieti P, Milner LA, Kronenberg H, Scadden DT. Osteoblastic cells regulate the hematopoietic stem cell niche. *Nature* 2003; 425:841-6.
96. Wang Z, Cohen K, Shao Y, Mole P, Dombkowski D, Scadden DT. Ephrin receptor, EphB4, regulates ES cell differentiation of primitive mammalian hemangioblasts, blood, cardiomyocytes and blood vessels. *Blood* 2004; 103: 100-9.
97. Willet CG, Boucher Y, di Tomaso E, Duda DG, Munn LL, Tong RT, Chung DC, Sahani DV, Kalva SP, Kozin SV, Mino M, Cohen KS, Scadden DT, Hartford AC, Fischman AJ, Clark JC, Ryan DP, Zhu AX, Blaszkowsky LS, Chen HX, Shellito PC, Lauwers GY, Jain RK. Direct evidence that the VEGF-specific antibody bevacizumab has antivascular effects in human rectal cancer. *Nature Medicine* 2004; 10: 145-147.
98. Qui J, Takagi Y, Rodrigues N, Moskowitz MA, Scadden DT, Cheng T. Regenerative response in ischemic brain restricted by p21Cip1/Waf1. *J Exp Med* 2004; 199: 937-45.
99. Chabner KT, Adams GB, Qui J, Moskowitz M, Marsters ES, Topulos GP, Scadden DT. Direct vascular delivery of hematopoietic cells to bone marrow improves localization, but not engraftment. *Blood* 2004; 103:4685-6.
100. Yuan Y, Shen H, Franklin DS, Scadden DT, Cheng T. In vivo self-renewing divisions of hematopoietic stem cells are increased in the absence of the early G1-phase inhibitor, p18<sup>INK4c</sup>. *Nature Cell Biology* 2004; 6(5):436-42.
101. Craiu A, Saito Y, Limon A, Eppich HM, Olson DP, Rodrigues N, Adams GB, Dombkowski D, Richardson P, Schlossman R, Choi PS, Grogins J, O'Connor PG, Cohen K, Attar EC, Freshman J, Rich R, Mangano JA, Gribben JG, Anderson KC, Scadden DT. Flowing cells through pulsed electric fields efficiently purges stem cell preparations of contaminating myeloma cells while preserving stem cell function. *Blood*. 2005;105(5):2235-8.
102. Suscovich TJ, Paulose-Murphy M, Harlow JD, Chen Y, Thomas SY, Mellott TJ, Walker BD, Scadden DT, Zeichner S, Brander C. Defective immune function of primary effusion lymphoma cells is associated with distinct KSHV gene expression profiles. *Leuk Lymphoma*. 2004;45(6):1223-38.
103. Noy A, Scadden DT, Lee J, Dezube BJ, Aboulafia D, Tulpule A, Walmsley S, Gill P. Angiogenesis inhibitor IM862 is ineffective against AIDS-Kaposi's sarcoma in a phase III trial, but demonstrates sustained, potent effect of highly active antiretroviral therapy: from the AIDS Malignancy Consortium and IM862 Study Team. *J Clin Oncol*. 2005;23(5):990-8. Epub 2004 Dec 14.

104. Kutok JL, Yang X, Folkerth RD, Imitola J, Raddassi K, Yano Y, Salahuddin S, Lawitts J, Imboden H, Chinami M, Shirakawa T, Turner H, Khoury S, Sayegh MH, Scadden D, Adra C. The cell cycle associated protein, HTm4, is expressed in differentiating cells of the hematopoietic and central nervous system in mice. *J Mol Histol.* 2005; 36(14):77-87
105. Rodrigues NP, Janzen V, Forkert R, Dombkowski DM, Boyd AS, Orkin SH, Enver T, Vyas P, Scadden DT. Haploinsufficiency of GATA-2 perturbs adult hematopoietic stem cell homeostasis. *Blood* 2005 (in press).
106. Stier S, Ko Y, Forkert R, Lutz C, Neuhaus T, Grunewald E, Cheng T, Domkowski D, Calvi LM, Rittling SR, Scadden DT. Matrix glycoprotein, osteopontin, is a niche constituent that negatively regulates hematopoietic stem cell pool size. *J Exp Med.* 2005; 201:1781-1791.
107. Zhang JL, Attar E, Cohen K, Crumpacker C, Scadden DT. Silencing p21 Waf1/Cip1/Sdi1 expression increases gene transduction efficiency in primitive human hematopoietic cells. *Gene Therapy* (in press).
108. Zong JL, Zack Z. Wang, Yi Zhou Zheng, Bin Xu, Ren Chi Yang, David T. Scadden, Zhong Chao Han. Kinetic expression of platelet endothelial cell adhesion molecule-1 (PECAM-1/CD31) during embryonic stem cell differentiation. *J Cellular Biochemistry* 2005;95:559-570.
109. Woodberry T, Suscovich TJ, Henry LM, Martin JN, Dollard S, O'Connor PG, Davis JK, Osmond D, Lee T, Kedes DH, Khatri A, Lee JY, Walker BD, Scadden DT, Brander C. T cell responses to KSHV ORF73 and ORF65. *J. Inf. Dis.* (in press).
110. Stroh M, Zimmer JP, Duda DG, Levchenko TS, Cohen KS, Brown EB, Scadden DT, Torchilin VP, Bawendi MG, Rukumura D, Rain RK. Quantum dots spectrally distinguish multiple species within the tumor milieu *in vivo*. *Nature Med.* 2005;11:678-82.
111. Woodberry T, Suscovich TJ, Henry LM, Davis JK, Frahm N, Walker BD, Scadden DT, Wang F, Brander C. Differential targeting and shifts in the immunodominance of EBV specific CD8 and CD4 T cell responses from acute to persistent infection. *J. Inf. Dis.* (in press).
112. Kaplan LD, Lee JY, Ambinder RF, Sparano JA, Cesarman E, Chadburn A, Levine AM, Scadden DT. Rituximab does not improve clinical outcome in a randomized phase III trial of CHOP with or without rituximab in patients with HIV-associated non-Hodgkin's lymphoma: AIDS-malignancies consortium trial 010. *Blood* 2005 (in press).

### **Proceedings of Meetings**

1. Scadden DT. Granulocyte macrophage colony stimulating factor (GM-CSF) in AIDS. In: Spivak J, Drohan W, Dooley D, eds. *Hematopoietic Growth Factors in Transfusion Medicine. Proceedings of the XXth Annual Scientific Symposium of the American Red Cross, Bethesda, Maryland, May 10-11, 1989. Progress in Clinical and Biological Research, Volume 338, Wiley-Liss, Inc. New York, p163-176.*

2. Scadden DT, Bering HA, Levine JD, Bresnahan J, Evans L, Epstein C, Groopman JE. GM-CSF as an alternative to dose modification of combination Zidovudine and Interferon- $\alpha$  in the treatment of AIDS-associated Kaposi's sarcoma. In: Brady LW, ed. Am. J. Clin. Oncol. Proceedings of the Satellite Symposium to the 15th UICC Congress, Hamburg, F.R.G., August 18, 1990. Cytokines in Tumor Therapy (GM-CSF, G-CSF, and IL-3), Volume 14 (Suppl 1), Raven Press, New York, pS40-S44.
3. Groopman JE, Sakaguchi M, Scadden DT. Pathogenesis of HIV mediated blood cell abnormalities. In: Girard M, Valette L, eds. Retroviruses of human AIDS and related animal diseases. Proceedings of the Cinquieme Colloque Des Cent Gardes Meeting, October 1990. Foundation Merieux, Paris, France. p5-8, 1991.
4. Scadden DT, Krown SE, Gill PS. Hematologic and oncologic complications of HIV disease. In: Menitove JE, McArthur Jr, eds. Education Program, American Society of Hematology, 34th annual meeting, Anaheim, California, December 5-8, 1992. p120-126.
5. Golde DW, Neidhart JA, Scadden DT, Nimer SD. The rational use of hematopoietic growth factors. In: Section Seven: Special Topics. Education Program, American Society of Hematology, 37th annual meeting, Seattle, Washington, December 1-5, 1995. p112-118.
6. Scadden DT. Cytokine use in the management of HIV disease. In: HIV Infection and AIDS: New Biology, Therapeutic Advances, and Clinical Implications. XI International Conference on AIDS. Vancouver, British Columbia, Canada, July 8, 1996. Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology. 16: (suppl 1) pS23.
7. Scadden DT. Hematologic aspects of HIV disease and immune reconstitution. Education Program, American Society of Hematology, 41<sup>st</sup> annual meeting, New Orleans, Louisiana, December 3-7, 1999.
8. Levine AM, Scadden DT, Zaia JA, Krishnan A. Hematologic aspects of HIV/AIDS. In: Hematology, American Society of Hematology Education Program, 42<sup>nd</sup> Annual Meeting, Orlando, FL, December 6-12, 2001. p463-78.
9. Scadden DT, Shen H, Cheng T. Hematopoietic stem cells in HIV disease. J Natl Cancer Inst Monogr 2001; (28):24-9
10. Scadden DT. AIDS-related lymphoma. In: American Society of Clinical Oncology 2002 Educational Book, 38<sup>th</sup> Annual Meeting, Orlando, FL, May 18-21, 2002. P266-272.

#### **Review Articles, Chapters and Editorials:**

1. Groopman JE, Scadden DT. Interferon therapy for AIDS-related Kaposi's sarcoma. Ann Intern Med. 1989;110:335-337.
2. Groopman JE, Molina JM, Scadden DT. Hematopoietic growth factors: biology and clinical applications. N Engl J Med. 1989;321:1449-1459.

3. Scadden DT, Zon L, Groopman JE. Pathophysiology and management of HIV-associated hematologic disorders. *Blood*. 1989;74:1455-1463.
4. Scadden DT, Feder D, Groopman JE. Scratching the surface: Kit ligand and hematopoiesis. *Current Biology* 1991;1:301-303.
5. Scadden DT. The Use of GM-CSF in AIDS. *Infection*. 1992;20(S2):S103-S106.
6. Scadden DT. The clinical applications of colony-stimulating factors in acquired immunodeficiency syndrome. *Semin Hematol*. 1992;29(4):33-37.
7. Freedman AR, Scadden DT. Viral activity in early HIV disease. *Current Opinion in Hematology* 1994;1:19-23.
8. Scadden DT, Groopman JE. AIDS. In: Handin RI, Lux SE, Stossel TP, eds. *Blood: Principles and Practice of Hematology*. Philadelphia: J.B. Lippincott Company, 1994:697-726.
9. Scadden DT, Groopman JE. AIDS-associated lymphoma. In: Hoffman R, Benz EJ, Shattil SJ, Furie B, Cohen HJ, Silberstein LE, eds. *Hematology: Basic Principles and Practice*, 2nd edition. New York: Churchill Livingstone 1994:1344-1353.
10. Scadden DT, Groopman JE. Acquired immune deficiency syndrome. In: Wyngaarden JB, Smith LH, Bennett JC, Plum F, eds. *Cecil Textbook of Medicine* 20th edition. Philadelphia: WB Saunders, 1996:1870-1875.
11. Scadden DT, Freedman AR. GM-CSF in the treatment of AIDS. *Marty: Manual of GM-CSF*: United Kingdom: Blackwell Science Ltd. 1996:181-193.
12. Scadden DT, Golde D. Growth factors in the treatment of disease. In: Gupta, ed. *Immunology of HIV Infection*. Plenum Press: 1996:525-531.
13. Scadden DT, Ellis MH. AIDS-associated malignancies. In: Skarin, AT, ed. *Mosby-Wolfe Atlas of Diagnostic Oncology* 2e. 1996:577-588.
14. Scadden DT, Fairchild, PG. HIV-associated malignancies. In: Forti DQ, ed. *American Cancer Society, 9th edition. Cancer Manual*. 1996:525-534.
15. Scadden, DT. Hematologic Disorders and Growth Factor Support in HIV Infection. In: *Hematology/Oncology Clinics of North America*. 1996;10:1149-1161.
16. Scadden DT. Cytokine Use in the Management of HIV Disease. In: Miles S, ed. *J Acq Imm Def Synd & Human Retro*. 1997;16(Supp.1):S23-S29
17. Scadden DT, Groopman JE. Hematology/Oncology in AIDS. In: Goldman L & Bennet JC, editors. *Cecil Textbook of Medicine*, 21<sup>st</sup> edition. 1998.

18. Scadden DT. Mother knows best: New developments in Kaposi's sarcoma. *Nature Medicine*. 1998;4:390-392.
19. Scadden DT, Howard W. AIDS-related malignancies. In: *The Oncologist*. AlphaMed Press. 1998;3:119-123.
20. Scadden DT. Cytopenias associated with HIV-1 and other infections. In: Ganser A, Hoelzer D, eds. *Cytokines in the treatment of hematopoietic failure*. Marcel Dekker, Inc. 1998.
21. Scadden DT. Non-Hodgkin's lymphoma future targets for prevention and therapy. In: Feigal, Levine, Biggar, eds. *AIDS-related Cancers and Their Treatment*. 1998.
22. Scadden DT. Management of AIDS-associated Kaposi's sarcoma: A multidisciplinary Perspective. In: *Center for Bio-Medical Communication*. 1998.
23. Scadden DT, Groopman JE. AIDS-associated lymphoma. In: Hoffman R, Benz EJ, Shattil SJ, Furie B, Cohen HJ, Silberstein LE, eds. *Hematology: Basic Principles and Practice*, 3rd edition. New York: Churchill Livingstone 1998.
24. Scadden DT. AIDS-related malignancies. In: *Curr Opin Oncol* 1998;10: 403-404.
25. O'Connor P, Scadden DT. Hodgkin's Disease. In: Goedert JJ, ed. *Infectious Causes of Cancer: Targets for Intervention*. 1999.
26. Scadden DT. AIDS-related non-Hodgkin's Lymphomas. In: Mansur H, Dolin R, Saag M, editors. *AIDS Therapy*, 1<sup>st</sup> edition. 1999.
27. Scadden DT. Hematologic Aspects of HIV Disease and Immune Reconstitution. In: *ASH Education Book, Hematology* 1999.
28. Scadden DT. Immune reconstitution in AIDS: oncologic implications and hematologic approaches. In: *Current Opinion in Oncology*. Lippincott Williams & Wilkins, Inc., 1999;11:503-507.
29. Friel TJ, Scadden DT. Hematologic manifestations of HIV infection: Thrombocytopenia and coagulation abnormalities. In: Burton D, Rose MD, eds. *UpToDate, Inc.* <<http://www.uptodate.com>> 2000.
30. Friel TJ, Scadden DT. Hematologic manifestations of HIV infection: Anemia. In: Burton D, Rose MD, eds. *UpToDate, Inc.* <<http://www.uptodate.com>> 2000.
31. Levine AM, Scadden DT, Zaia JA, Krishnan A. Hematologic Aspects of HIV/AIDS. *Hematology (Am Soc Hematol Educ Program)* 2001; 463-78
31. Friel TJ, Scadden DT. Hematologic manifestations of HIV infection: Neutropenia. In: Burton D, Rose MD, eds. *UpToDate, Inc.* <<http://www.uptodate.com>> 2000.

32. Scadden DT. Non-Hodgkin's lymphoma: Future targets for prevention and therapy. In: Feigal, Levine, Biggar, eds. *AIDS-related Cancers and Their Treatment*. New York: Marcel Dekker, Inc; 2000. p. 195-207.
33. Evans RH, Scadden DT. Haematological aspects of HIV infection. In: *Bailliere's Best Practice and Research: Clinical Haematology*. London, U.K., Bailliere Tindall, 2000;13:215-230.
34. O'Connor PG, Scadden DT. AIDS Oncology. In: *Infectious Disease Clinics of North America*. Philadelphia, PA, W.B. Saunders Company, 2000;14:945-65.
35. Whelan P, Scadden DT. New developments in the etiopathogenesis and treatment of HIV-related Kaposi's sarcoma. In: *Clinics in Dermatology*. New York, NY, Elsevier Science Inc., 2000;18:469-77.
36. Scadden DT. Neoplasms in acquired immunodeficiency syndrome. In: Holland JF, Frei E, Bast RC, Kufe DW, Pollack RE, Weichselbaum RR, eds. *Cancer Medicine*, 5<sup>th</sup> Edition. Ontario, Canada, B.C. Decker, Inc., 2000;37:2099-114.
37. Scadden DT. Epstein-Barr Virus, the CNS, and AIDS-related lymphomas: As close as flame to smoke [editorial]. *J Clin Oncol* 2000;18:3323-4.
38. Scadden DT, Shen H, Cheng T. Hematopoietic stem cells in HIV disease. *J Natl Cancer Inst Monogr* 2000;28:24-9.
39. Cohen K, Scadden DT. Non-Hodgkin's lymphoma: pathogenesis, clinical presentation, and treatment. In: Sparano J, ed. *HIV & HTLV-I Associated Malignancies*. Norwell, MA, Kluwer Academic Publishing, 2001;7: 201-230.
40. Poznansky MC, Scadden DT, Luster AD. Chemokine and chemokine receptor analysis. In: Rose NR, Hamilton RG, Detrick B, editors. *Manual of Clinical Laboratory Immunology*, 6<sup>th</sup> Edition. Washington, DC, ASM Press. 2002; 357-367.
41. Scadden DT. Acquired Immunodeficiency Syndrome. In: Handin RI, Lux SE, Stossel TP, eds. *Blood: Principles and Practice of Hematology*, 2<sup>nd</sup> Edition. Philadelphia, PA, Lippincott Williams & Wilkins. 2003; 2: 713-732.
42. Friedberg J, Scadden DT. Cancer and the Immunocompromised Host. In: Furie, Mayer, Cassileth, Atkins eds. *Clinical Practice of Hematology and Oncology: Presentations, Diagnosis, and Treatment*. Philadelphia, PA, Harcourt Health Sciences: W.B. Saunders, Mosby, Churchill Livingstone. 2003; 1155-1165
43. Cohen K, Scadden DT. AIDS-related non-Hodgkin's Lymphoma. In: Grossbard M, ed. *ACS Atlas of Clinical Oncology, Malignant Lymphoma*. Ontario, Canada, B.C. Decker Inc., 2002;241-258.

44. Scadden DT. Toward cellular-based therapies for HIV infection. *J Hematother Stem Cell Res.* Oct. 2002; 11:759-64.
45. Scadden DT. AIDS-Associated Malignancies. In: Skarin A, ed. *Atlas of Diagnostic Oncology*, 3<sup>rd</sup> Edition. London, United Kingdom, Harcourt Publishers Limited. 2003; 17:584-596.
46. Scadden DT. AIDS-related malignancies. *Annu Rev Med.* 2003;54:285-303.
47. Robertson P, Scadden DT. Immune reconstitution in HIV infection and its relationship to cancer. *Hematol Oncol Clin North Am.* 2003;3:703-16, vi.
48. Scadden DT. Non-Hodgkin Lymphoma. In: Dolin R, Masur H, Saag M, eds. *AIDS Therapy*, 2<sup>nd</sup> Edition. NY, New York, Churchill Livingstone, a Harcourt Health Sciences Company. 2003;51:696-705.
49. Scadden DT. AIDS-related neoplasms. In: Pollock R, ed. *UICC Manual of Clinical Oncology*, 8<sup>th</sup> Edition. New York, NY, John Wiley & Sons (in press).
50. Scadden DT. Hematology/Oncology in AIDS. In: Goldman L and Ausiello D, eds. *Cecil Textbook of Medicine*, 22<sup>nd</sup> Edition. Philadelphia, PA, Harcourt Health Sciences: W.B. Saunders, Mosby, Churchill Livingstone. 2003;419:2173-2177.
51. Scadden DT. Stem Cells and Immune Reconstitution in AIDS. *Blood Reviews.* 2003 Dec;17 4: 227-231. Invited commentary.
52. Scadden DT. AIDS lymphomas: beginning of an EPOCH? *Blood.* June 2003;101:4647. Invited commentary.
53. Whelan JP, Scadden DT. Lymphoma and abnormalities of the immune system. In: Mauch PM, Armitage JO, Harris NL, Coiffier B Dalla-Favera R, eds. *Non-Hodgkin's Lymphomas*, 1<sup>st</sup> ed. Philadelphia, PA, Lippincott, Williams & Wilkins, 2003;45:729-748.
54. Scadden DT. T-cell differentiation: Notch another step. *Blood.* Oct. 2003; 102: 2316 Invited commentary.
55. O'Connor PG, Scadden DT. Neoplastic Complications of HIV Infection. In: *AIDS & Other Manifestations of HIV Infection*. San Diego, CA, Academic Press. 2004;21:597-611.
56. Scadden DT, Groopman JE. AIDS-associated lymphoma. In: Hoffman R, Benz EJ, Shattil SJ, Furie B, Cohen HJ, Silberstein LE, McGlave P, eds. *Hematology: Basic Principles and Practice*, 4th edition. Philadelphia: Elsevier. 2004;82: 1487-1500.
57. Scadden DT, Attar, E. Stem cells. In: Gribben J, Provan D, eds. *Molecular Haematology*, 2<sup>nd</sup> edition. Oxford: Blackwell Publishing (in press).

58. Cheng T, Scadden DT. Cell Cycle Regulators in Stem Cells. In: Lanza, et. al, editors. Handbook of Stem Cells: Adult and Fetal Volume. Amsterdam: Elsevier. 2004 Aug; 2(6):73-82.
59. Scadden DT. The malignant side of successful transplantation. American Journal of Transplantation. 2004; 4: 153-4. Invited editorial.
60. Scadden DT. Cancer stem cells refined. Nat. Immunol. 2004 Jul;5(7):701-3. Invited commentary.
61. Attar EC, Scadden DT. Regulation of hematopoietic stem cell growth. Leukemia. 2004 18:1760-8.
62. Scadden DT. Cord blood transplantation: the complexity of success. The Hematologist: ASH News and Reports. 2004; 1,4:7.
63. Scadden DT. Book Review. Am J Transplant. 2005 Jan;5(1):193.
64. Fangman JJ, Scadden DT. Anemia in HIV-Infected Adults: Epidemiology, Pathogenesis, and Clinical Management. Curr Hematol Rep. 2005 Mar; 4(2):95-102.
65. Adams GB, Scadden DT. Microenvironmental influences on stem cell function. Discovery Medicine (in press).

#### **Patents:**

1. Scadden DT, Rosenzweig M, Johnson PR, inventors; President and Fellow of Harvard College assignee. In vitro differentiation of CD34+ progenitor cells into T lymphocytes. US patent 5,677,139. 1997 October 14.
2. Godowski PJ, Mark MR, Scadden DT, inventors; Genentech, Inc., New England Deaconess Hospital assignees. Antibodies specific for Rse receptor protein tyrosine kinase. US patent 5,709,858. 1998 January 20.
3. Scadden DT, inventor; Beth Israel Deaconess Medical Center, Inc. assignee. Method of selecting pluripotent hematopoietic progenitor cells. US patent 5,827,742. 1998 October 27.
4. Scadden DT, inventor; Beth Israel Medical Center, Inc. assignee. Method of screening a compound for hematopoietic activity. US patent 5,965,437. 1999 October 12.
5. Godowski PJ, Mark MR, Scadden DT, inventors; New England Deaconess Hospital, Genentech, Inc. assignees. Protein tyrosine kinases. US patent 6,001,621. 1999 December 14.
6. Scadden DT, Freedman A, inventors; Beth Israel Medical Center, Inc. assignee. In-vitro T-lymphopoiesis system. US patent 6,004,812. 1999 December 21.
7. Scadden DT, Baker, KP, Baron WF, inventors; Genentech, Inc. assignee. Protein tyrosine kinases. US patent 6,087,144. 2000 July 11.



8. Poznansky MC, Luster, AT, Scadden DT, inventors; The General Hospital Corporation assignee. Purposeful movement of human migratory cells away from an agent source. US patent 6,448,054. 2002 Sep 10.

## **APPENDIX B**

## siRNA

Si-2  
5' CUU CGA CUU UGU CAC CGA G 3'  
GAA GCU GAA ACA GUG GCU C

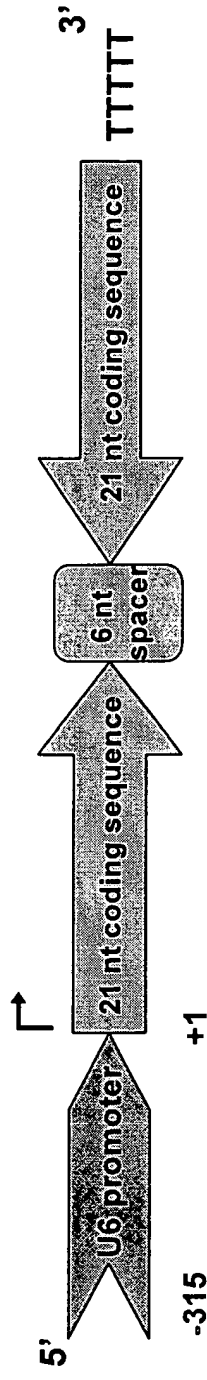
Si-2M  
5' CUC GAC UUC GUA CCC GAG 3'  
GAG CUG AAG CAU GGG CUC

HPRT  
5' GUG UCA UUA GUG AAA CUG G 3'  
CAC AGU AAU CAC UUU GAC C

## shRNA

Coding sequence

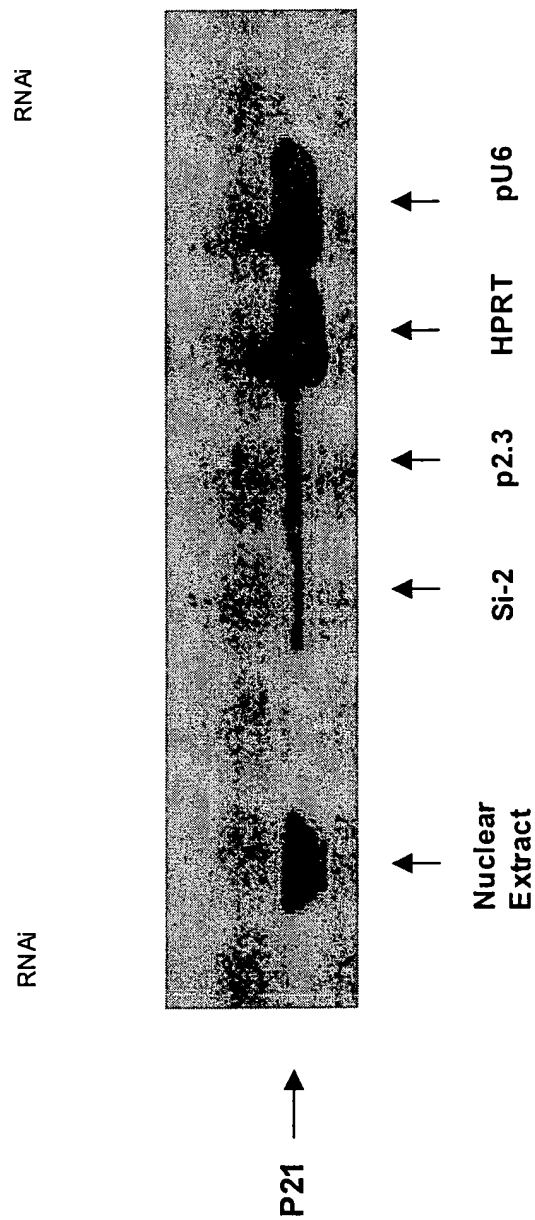
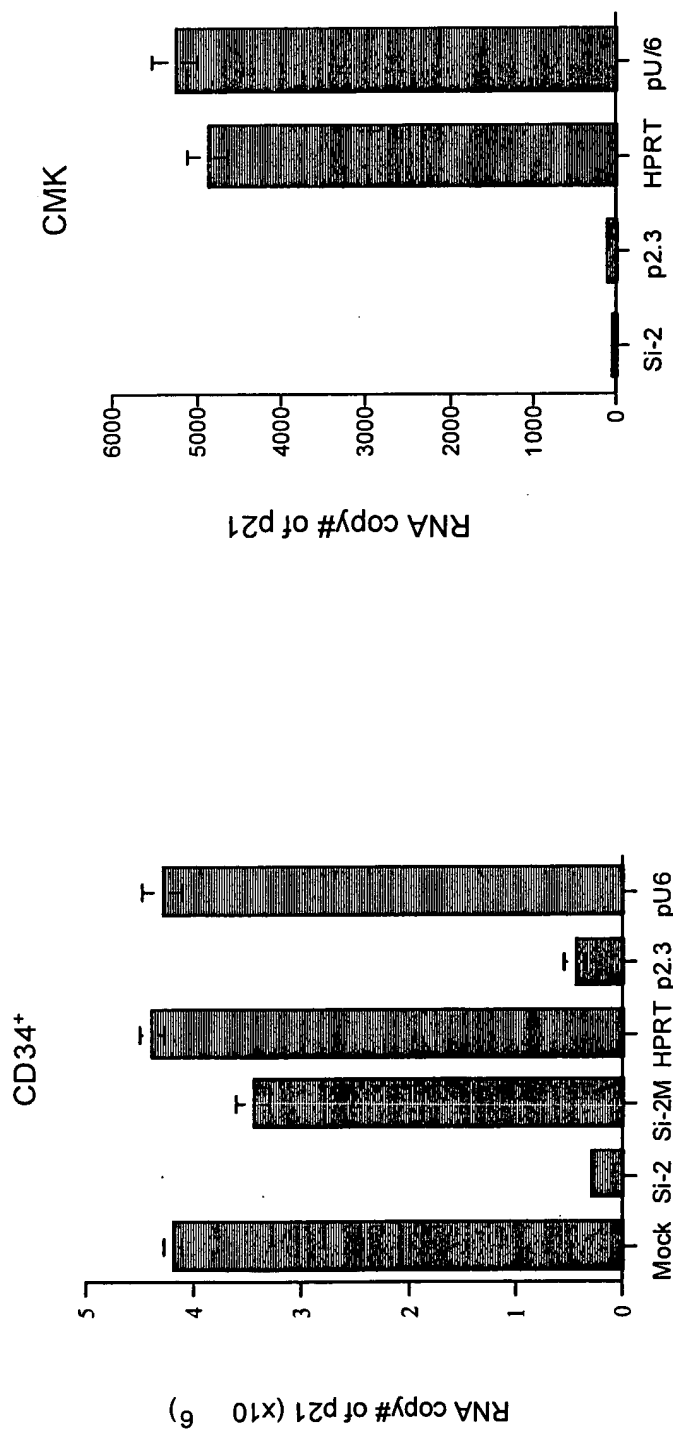
p2.3  
5' GGT GAC TTC GCC TGG GAG CGT ATC  
GTA ACG CTC CCA GGC GAA GTC ACC 3'



## p21 cDNA

1 cgtcagaacc catgcggcag caaggcdgc cgcgcctd: toggcccagt ggacagcgag  
61 cagdtgagcc gogadtgga tggdtaatg ggggdtgca toaggaggc ogtgagcga  
121 tggaaattog adtttcac cgaqacacca dtggagggtg atttccdtg ggaqcdgtg  
Si-2 p2.3  
181 cggggccttg gdcgccccaa gdtacdt oacacggggc oocggcgagg ccgggatgag  
481 ttocaggggtg acagtgagat toatdcaaa taaatacata aataaaaaac tgttggtaa  
541 tatdttd

## **APPENDIX C**



BEST AVAILABLE COPY

## **APPENDIX D**

